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REPORTS OF THE

CHEMICAL LABORATORY

OF THE

AMERICAN MEDICAL ASSOCIATION

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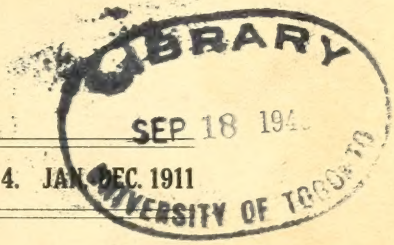

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W. A. PUCKNER

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VOLUME 4

JANUARY—DECEMBER, 1911

By W. A. PUCKNER
DIRECTOR OF THE LABORATORY

PRESS OF
AMERICAN MEDICAL ASSOCIATION
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PREFACE

The present volume includes reports of the work of the past year which has been carried out on the same lines as in previous years. The scope of this work is described in the preface of volume two.

In addition to the work growing out of the investigations of the Council, it includes the occasional examination of "patent medicines" and a considerable amount of investigation of chemical questions arising in connection with the Propaganda department of THE JOURNAL of the American Medical Association.

In conformity with previous reports, this volume contains an account of those portions of the laboratory's activities which it was thought would be of interest to drug analysts, i. e., those engaged in the examination of medicines. Those interested in this field of activity should consult the index, although the methods of analysis for Hesperian Tonic and Sulphume may be of particular value. The attention of teachers of materia medica and of chemistry who wish to discuss the adulteration and sophistication of drugs before their classes is called to the reports on Tablets of Bismuth, Opium and Phenol and Bismuth Iodo-Resorcin Sulphonate. The items on Plantoxine, En-Ar-Co Oil, Liquid Life, Mayr's Wonderful Stomach Remedy and Thacher's Worm Syrup should be noted by those who are interested in the enforcement of drug laws. The constructive work looking toward the establishment of standards for little used drugs, examples of which may be found in the studies on Dried Magnesium Sulphate, and Calcium Phenolsulphonate, should be familiar to dispensing

pharmacists, and, it is hoped, will also be considered by manufacturers. The working method given for the preparation of quinin tannate should be of direct value to pharmacists who wish to dispense that which is best on prescriptions, while the studies on incompatibilities (see index) should be of interest alike to prescribers and dispensers. The arrangement of the material is the same as in previous years, viz:

(*a*) Contributions of the Chemical Laboratory of the American Medical Association;

(*b*) Chemical Data contributed to THE JOURNAL by the Laboratory;

(*c*) Unpublished Work of the Laboratory.

CONTENTS

PART I.

REPRINTS OF CONTRIBUTIONS FROM THE CHEMICAL LABORATORY OF THE AMERICAN MEDICAL ASSOCIATION

PROPRIETARY MEDICINES IN THE UNITED STATES*

W. A. Puckner

Broadly speaking, medicaments may be divided into two classes, official remedies and proprietary remedies. In the first are those whose composition is known and which may be prepared by any competent chemist. In the other are proprietary medicines which are the property of an individual or of a firm either by protection secured under the patent law or the trade-mark law, or through secrecy of composition.

Proprietary medicines are of two kinds, those sold to the public and those intended for use by physicians—it being a common occurrence, however, that a medicine is first offered to the medical profession and later is exploited to the public as a cure-all.

In the United States, proprietary medicines sold to the public are commonly called "patent medicines", though as a matter of fact, most of them are not patented but are proprietary only because the name is trade-marked and their composition is secret. The traffic in these so-called "patent medicines" which are better designated as "nostrums," is so extensive that a leading magazine, *Collier's Weekly*, in a crusade against them, referred to them under the caption "The Great American Fraud." The amount of suffering and the number of deaths which these nostrums have caused, both directly by the use of dangerous drugs and indirectly by keeping the sick from consulting qualified persons is hard to imagine. Since the daily papers and the magazines derive a large part of their income from the advertisements of nostrums, many editors are afraid to publish anything which might be considered derogatory to

* Reprinted from "Progress," London, England, April, 1911.

any of the preparations named in their advertising pages. The nostrum interests have even gone so far as to force editorial opposition to any proposed legislation aimed to correct the "patent medicine" abuses on pain of withdrawing all advertising contracts. Hence, it has been most difficult to apprise the public of the harmful effects of nostrums. However, a number of forces are at work to curb the evil, the most noteworthy being the United States Postoffice Department, the officials charged with the enforcement of the federal "Food and Drugs Act" and the American Medical Association. The Postoffice Department usually proceeds by proving that the nostrum or treatment will not accomplish what it is claimed to do and that, therefore, the mails are being used to transact business that is fraudulent. In the past the action taken has been the issuance of a "fraud order" which debars the concern from receiving any mail and thus stops most effectually the transaction of its business. As the legal formalities under which such an order is obtained are very simple these proceedings have done much good. But as such an order does not prevent the party affected from embarking in another business under another name, the postal authorities have announced their intention to hereafter supplement the issuance of a fraud order by criminal prosecution which will place the offenders behind the bars. The federal "Food and Drugs Act" except in the case of dangerous, habit-forming drugs, does not require that the ingredients be declared, but does require that no untruthful statements shall be made on the labels of the remedies and directs the enforcement of this provision. As such remedies have little sale when the truth and the truth only is told about them, many infractions of the law are brought before the courts, and in this way the traffic in nostrums is being very much curtailed.

The American Medical Association has devoted itself in the main to the correction of frauds practiced on the medical profession and has taken up nostrums sold to the public only when it considered them a serious menace to public health. The Association's plan of procedure depends entirely on educational methods—that is, in bringing the facts to the attention of the medical profession and also to that of the public when deemed necessary. The Association's journal has a subscription list of about 60,000. It accepts no advertisements unless they are truthful and it speaks fearlessly and independently in its pages. Its analyses of nostrums have, in some cases, been made the basis of prosecutions by the government. As

an illustration of the difference between medical journals here and in England it may be well to note that a preparation which the American Medical Association has shown to be fraudulent and which has been held to be misbranded by the United States courts is to-day advertised in the London *Lancet* under its fraudulent name "Waterbury's Metabolized Cod Liver Oil." As an illustration of the extremes to which exploiters of nostrums have gone in this country, the following example may be of interest: Of all nostrums the so-called "baby syrups" are perhaps the most harmful. While the mother is encouraged to give such preparations to her child on all occasions, the nostrums are almost without exception, solutions of morphin or opium. Besides being often the direct cause of death through an overdose their continued use, even in small doses, casts a veritable blight over a child's life. While there are a host of these syrups on the market "Winslow's Soothing Syrup" and Kopp's Baby's Friend" are best known. The "Food and Drugs Act" now requires that the morphin content of medicinal preparations be declared on the label, and at the same time the public is being advised of the actual cases of death due to their use as well as of their deleteriousness even when used in small amounts. The "headache cures" are another class of dangerous nostrums. In the past they have nearly always contained acetanilid (also known as antifebrin) and their promiscuous use has shattered many a constitution. Now, however, the law requires the amount of acetanilid in any preparation to be declared on the label, and as the public is being educated in regard to the harmful effects of this drug, its use is being considerably curtailed. Most profitable, but also most cruel, are those "patent medicine" concerns which prey on the incurables—the consumptives, the sufferers from cancer, etc. Beyond promises of cures which are impossible, they often rob the sufferer of his last savings and hasten his death by depriving him of proper medical care. As illustrations may be mentioned "Lung Germine" which consists of sulphuric acid, alcohol and water, which sold at the rate of $5.00 (£1 - 0 - 0) for a 2-ounce bottle. "Sartolin," a "consumption cure" also exploited in England, consists of sulphur, charcoal and eucalyptus. The user of "Sartolin" is directed to burn some of it in a room having the windows closed tightly and to sleep in the vile atmosphere thus produced. Thus the sufferer is deprived of that which he needs more than anything else, a good supply of fresh air. Some of the methods which are made use of to

part the fool from his money though vicious in that they keep the dupe from seeking competent advice, and in this way always potent for much harm are really ludicrous in the way that they avail themselves of human credulity. The following are illustrations which may be of interest in this connection: "Professor Samuels' Eyewater" is said to cure such things as consumption, fits, paralysis, eczema, Bright's disease, morphin habit and heart trouble. It is said to sell at $25.00 (£5-0-0) an ounce. According to an analysis made in the chemical laboratory of the American Medical Association it appears to be a solution of common salt and sugar which could be produced for 6 cents (3 pence) a gallon. While the impossibility of effectively treating the diseases named by applications to the eye, should be evident to all, nevertheless "Professor" Samuels apparently found many dupes. "Fruitola" is said to be a gall-stone remedy. It consists of a bottle containing about ½ pint of olive oil which is taken at a single dose, and is followed by a liberal dose of Seidlitz powders. The oil in passing through the intestines is changed to solid masses of soap which are then carried off by the Seidlitz powders. The poor dupe is led to believe that these soapy secretions are gall-stones. It is needless to say that gall-stones cannot possibly be removed by a purgative. While this remedy is sold at $1.00 (4 shillings) a dose, some fakers make use of the same idea but charge their victims a dollar for every "gall-stone" which is expelled by the treatment.

The appliances known as "Oxydonor," "Oxygenor King" and "Oxygenator" are very closely allied. While they are most ridiculous humbugs, their exploitation has been so successful that they are now sold in almost every country on the globe, including England. The "Oxygenor King" was examined in the chemical laboratory of the American Medical Association and found to be a piece of nickel-plated brass pipe filled with a mixture of sulphur, sand and charcoal, and provided with two insulated wires. As the analyst puts it: "The fool—save the mark—ties one wire to his wrist and the other to his ankle and thus prepares himself for sleep." During this sleep he is to receive the wonderful, vitallizing, life-giving currents which are supposed to be created, but which, of course, are not, by the sulphur-charcoal-sand-wire combination. The method of selling the humbug is delightfully ingenious and shows that the sellers fully appreciate the effect of the mind on many real or imaginary ailments. Briefly, the instrument

is sent to anyone who will deposit $25.00 (£5 - 0 - 0) with a third party with the agreement that at the end of a certain time the money is to be released and go to the exploiters, or else that the instrument is to be returned. It is needless to say that this method is an eminent success. As the instrument can no doubt be produced for less than $1.00 (4 shillings) the profits accruing from those not returned is sufficient to net a handsome income to the promoters. While in the past the United States has been known as the land of "patent medicine" humbugs, conditions have now changed, thus the "patent medicine" men know quite well that things which cannot be sold with safety here, may be sold with impunity in England. As an illustration—it was recently brought to my notice that an American firm which had bought the right to sell an English nostrum in this country was forced to issue new advertising circulars because, as the firm stated, these circulars "would not go here." Their untruthfulness would soon bring the promoters into the toils of the "Food and Drugs Act."

It is to be hoped that the present agitation in England will result in legislation which will curb "unqualified practice" in every form.

THE PHYSICIAN AND THE PHARMACIST

W. A. Puckner

Physicians need pharmaceutical advisers—those whom they may consult concerning desirable methods of preparing medicines for administration, their incompatibilities and similar questions, on which it is difficult for physicians to keep posted. During recent years many physicians have been inclined to forsake their corner druggist, because he has been tried and too often found wanting, and have pinned their faith to pharmaceutical manufacturers and promotors of specialties and their detail men. Dependence on the specialty proprietors has, however, been disastrous—so disastrous that well informed physicians will have no more of the detail man.

The recent reports of the Council on Pharmacy and Chemistry of the American Medical Association and of the Association's chemical laboratory demonstrate amply that entire dependence cannot be placed on manufacturing pharmacists

[a] Read before the December meeting of the Washington branch of the American Pharmaceutical Association.

and their endless assortments of readymade tablets, elixirs and syrups.

While it has not been the aim of the American Medical Association in its propaganda for honest medicines to specially favor the retail pharmacist and to work in his interests, its publications are such that the retail pharmacist could use a large part of them as arguments that he deserves the confidence of the practicing physician. The recent reports from the Association's chemical laboratory giving the results of examinations of Tablets of Bismuth, Phenol and Opium and of certain Compound Digestive Tablets might well be used by the pharmacist as an argument to physicians, that instead of using the thousand and one ready made tablets offered by manufacturers, it would be to the advantage of the physician as well as the patient if he would prescribe remedies to be put up by the pharmacist. Again, the reasons given by the Council on Pharmacy and Chemistry for not recognizing the chemical substance, quinin arsenate, can be used by the pharmacist as another argument why the physician should write prescriptions. Quinin arsenate, it should be stated, was rejected by the Council because it was held that this compound containing both quinin and arsenic was such that it could not be used in quantity to get an efficient dose of quinin without getting too much arsenic, or if used for its arsenate value, its quinin content was too small to be of any use. Instead, it was suggested that physicians had better combine quinin and arsenic in their prescriptions in the quantities that are adapted to the needs of the individual patients. While quinin arsenate is a definitely chemical substance the arguments given against its use will apply to most proprietary mixtures. As another illustration of the possibilities which lie before pharmacists, a recent discussion in *The Journal* of the American Medical Association regarding the investigation of ergot preparations carried out by Edmunds and Hale in the Hygienic Laboratory of the United States Public Health and Marine Hospital Service may be taken. This examination showed in the first place that the proprietary preparations of ergot claimed to be wonderfully reliable, potent and permanent, possessed none of these qualities. The examination further showed that fluid extracts made by different firms, although claimed to have been standardized physiologically, on the whole did not compare favorably with a fluid extract made in a small way by the authors. It is interesting to note that *The Journal* of the American Medical Association in commenting on this work editorially, suggested that

> "Such results suggest that a reliable pharmacist following the official method may be able to supply the physicians with as good preparations as the large manufacturing houses, or even better."

In other words, the editor evidently believes that the time when the pharmacist might with advantage make his own fluid extracts has not passed, even in the case of such a drug as ergot.

Happily, there are signs that pharmacists are awake to the tendency of the times and are making efforts to devote more attention to the professional side of their profession; and, as a result, there is a tendency on the part of physicians to go back to the old times, and once more get in touch with their druggists. The pharmacist, however, must realize that physicians need *real pharmacists* as advisers and not druggists, who, while prominent at "Get-together dinners" with talk of "U. S. P. and N. F. Propaganda" neglect their prescription counters to prepare grewsome "patent-medicine" displays and advertising dodges in their front windows.

An illustration that pharmacists do not always appreciate the needs and demands of physicians was given some time ago by an editorial discussion in a drug journal in which was lauded as a shining light, one of the class of druggists who would "work" the doctor as did the detail man in the past. This drug-seller decorated his front window with a sign which read:

> "IF YOU HAVE NO FAMILY PHYSICIAN,
> LET US RECOMMEND ONE."

To supply the desired name of the proposed physician to the unwary passer-by who might be attracted by the sign, this seller of drugs placed the names of all doctors in his neighborhood on cards, shuffled them and then "dealt," so to say, "from the top of the deck" when his advice was asked. The drug journal says:

> "The list of doctors in the store includes about a score of names and addresses of efficient physicians residing in the vicinity of the store, and, in recommending them, a system of rotation and alternation is employed. Having recommended one doctor, the clerk crosses off that physician's name, and when the next request for a good physician is made, he selects the doctor whose name appears next on the list."

It appears that the drug seller feels proud of this Paris-like judgment and the drug journal apparently believed that physi

cians were devoutly thankful for the recommendation thus given. This much may be said of this seller of drugs: His advice is on a par with that which he gives when he recommends a "patent medicine" the composition of which he is ignorant, for a disease that he does not understand.

The plan proposed by this druggist is, of course, an insult to the medical profession and it is evident that this has been generally appreciated, for the scheme does not appear to have found favor.

I am convinced that physicians fully appreciate the help which pharmacists can give them and it only remains for the individual pharmacist to go to the individual physician and demonstrate that he is the one that may be relied on. This plan of procedure, I am sure, promises much good both for the pharmacist and the physician, and is my excuse for presenting this thought at this time.

BISMUTH IODO-RESORCIN SULPHONATE

W. A. Puckner and L. E. Warren

(*Reprinted, with additions, from The Journal A. M. A., Feb. 11, 1911, p. 441*)

Some time ago a proprietary preparation (in the form of suppositories) which was said to contain bismuth iodo-resorcin sulphonate as its chief ingredient, was refused recognition by the Council because, among other things, the claims made in regard to its composition were not substantiated by the firm which sold it. Subsequently the results of the examination of this product in the Association laboratory were published,[1] and it was shown that the preparation contained only negligible amounts of iodin and hence could not possibly contain more than very small amounts of bismuth iodo-resorcin sulphonate.

A similar preparation was recently submitted to the Council with the claim that it contained bismuth iodo-resorcin sulphonate as its essential constituent. In accordance with its usual procedure the Council considered this constituent at the same time that the preparation containing it was taken up.

The formula assigned by the manufacturer to this substance is as follows:

$$[C_6H_2(OH)_2ISO_3]_3Bi.3Bi(OH)_3$$

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1. Anusol Hemorrhoidal Suppositories: THE JOURNAL A. M. A., Oct. 2, 1909, p. 1112.

Bismuth iodo-resorcin sulphonate apparently is not described in chemical literature. The manufacturer of the specimen examined stated, however, that the process for the manufacture of the substance was "the subject of a patent application" by the firm. The potassium salt, from which the bismuth salt is said to be prepared, has been obtained in the form of microscopic crystals containing three molecules of water of hydration.[2]

$$KC_6H_2(OH)_2ISO_3+3H_2O$$

THE QUESTIONS INVOLVED

The points involved in the examination which is here reported have been classified as follows, for the purpose of bringing out the matter more clearly:

1. From the formula submitted by the manufacturer it was calculated that the bismuth salt should contain 19.69 per cent. of iodin and 43.17 per cent. of bismuth.

2. From the formula found in the literature it was also calculated that the potassium salt should contain 31.079 per cent. iodin and 13.22 per cent. of water.

3. In the first examination we reported finding but about 10 per cent. of iodin in the bismuth salt (in which 19.69 per cent. of iodin had been claimed) and about 50.6 per cent. of bismuth, an amount considerably larger than that indicated by the formula.

4. We also reported finding about 28.06 per cent. of iodin in the firm's specimen of potassium iodo-resorcin sulphonate in which, if the formula were correct, there should have been 31.079 per cent.

THE FIRM'S REPLY

These facts, substantially as given, were submitted to the firm which replied to the points raised as follows:

1a.—The theoretical iodin content of the firm's bismuth salt was 20.76 per cent. and its bismuth content was 45.36 per cent.

2a.—The potassium salt contained no water of hydration and theoretically should, therefore, contain 35.84 per cent. of iodin.

3a and 4a.—The method used by the Association laboratory for the determination of iodin was not a standard one in chemical literature since it gave but about 70 per cent. of the total iodin present. After the firm had reexamined a portion of the original specimen, it reported that by its method it had

2. Fischer: Monatschr. f. Chem., ii, 1881, 340.

found 14.2 per cent. iodin. According to the formula it should have contained 19.69 per cent. iodin, although the Association chemists had found but about 10 per cent. iodin. The firm stated that in the earlier examinations of its product a reagent had been used which was afterward found to contain large amounts of chlorin. In making the iodin estimations this chlorin was weighed as (silver) iodid with consequent erroneous results, no control estimations, evidently, having been made.

REEXAMINATION BY THE LABORATORY

Our calculations of the theoretical iodin and bismuth content in bismuth iodo-resorcin sulphonate having been challenged, the values were recalculated. This recalculation showed that the values first reported were correct and that the firm's challenge was unwarranted.

Our findings concerning the iodin content in bismuth iodo resorcin sulphonate also having been challenged, the iodin in the original specimen was redetermined by several independent methods. The highest result obtained by any method was 11.59 per cent. iodin. Although somewhat higher than that obtained by the method previously used, it is still considerably less than was claimed by the firm in its reexamination, viz., 14.2 per cent. An appreciable quantity of chlorin was also found, which may explain, at least in part, the firm's wrong estimate of its product.

On reexamining the potassium salt we found 32.00 per cent. of iodin and 10.41 per cent. of water—this notwithstanding the fact that the firm had asserted that its product contained no water of hydration.

A review of the above facts shows that the contentions of the firm could not be substantially confirmed. To summarize:

SUMMARY

1. The firm's claim that the laboratory's calculations were wrong is shown to be unfounded.

2. The firm's statement that its potassium salt of iodo-resorcin sulphonic acid contained no water of hydration is shown to be wrong, the salt, in fact, containing more than 10.0 per cent. of water.

3. The contention of the firm that the first method of analysis used by the Association laboratory gives low results is correct. The assertion is, however, not justified that the method gives but 70 per cent. of the iodin present since the amount first reported by us is about 88 per cent. of the amount found later.

The accompanying table gives in graphic form the essential points of the controversy.

	According to firm's formula or formula in literature.	According to analysis of Association chemists.	According to the firm's revised statements.	According to the check analysis of Association chemists.
Iodin content in bismuth salt ...	19.69 *	10.00	20.76 § / 14.20	11.59
Bismuth content in bismuth salt ...	43.17 *	50.60	45.36 §	No analysis made.
Iodin content in potassium salt..	31.079 †	28.06	35.84	32.00
Water of hydration in potassium salt	13.22 †	No analysis.	0.0	10.41

* Based on formula given by firm.
† Based on formula given in literature.
§ These figures were later acknowledged by the firm to be incorrect.

Details of Analysis

FIRST EXAMINATION

IODIN CONTENT OF BISMUTH IODO-RESORCIN SULPHONATE: A weighed portion of the material was placed in a flask and boiled with concentrated alcoholic potassium hydroxid. The mixture was diluted with water and the alcohol removed by distillation. Sufficient concentrated sulphuric acid was then slowly added to neutralize the alkali and bring the concentration of acid to about 5 per cent. About 5 gms. of ferric ammonium sulphate were added and the iodin distilled into a solution of potassium iodid, according to the method described in Sutton's "Volumetric Analysis," Ed. 8, p. 231. The iodin was then titrated with tenth-normal sodium thiosulphate using starch test-solution as indicator.

1 c.c. N-10 $Na_2S_2O_3$=0.01259 gm. I.

Results: The iodin distilled from 1.0451 gm. of the material required 8.43 c.c. tenth-normal sodium thiosulphate, equivalent to 0.10613 gm. iodin, or 10.15 per cent. The iodin distilled from 0.7389 gm. of the material required 5.83 c.c. tenth-normal sodium thiosulphate, equivalent to 0.0734 gm. iodin, or 9.94 per cent.; average, 10.05 per cent. iodin, or about 51.04 per cent of the amount indicated by the formula.

IODIN CONTENT OF POTASSIUM IODO-RESORCIN SULPHATE: The iodin distilled from 0.3402 gm. of the material required 7.55 c.c. tenth-normal sodium thiosulphate, equivalent to

0.095054 gm. iodin, or 27.94 per cent. The iodin distilled from 0.5409 gm. of the material required 12.11 c.c. tenth-normal sodium thiosulphate, equivalent to 0.152465 gm. iodin, or 28.19 per cent.; average, 28.06 per cent. iodin.

Bismuth Content of Bismuth Iodo-Resorcin Sulphonate: A portion of the material was dissolved in warm, concentrated hydrochloric acid, the solution diluted with hot water and saturated with hydrogen sulphid. The precipitate was collected on a filter, washed with hydrogen sulphid water and dissolved in warm diluted nitric acid. An excess of ammonia water, followed by a few drops of ammonium carbonate solution, was added to the solution and, after twenty-four hours, the precipitate was collected, dried, heated to redness and weighed as bismuth oxid.

Results: From 0.2964 gm. of the material 0.1676 gm. bismuth oxid was obtained, equivalent to 0.150297 gm. bismuth, or 50.71 per cent. From 0.2131 gm. of the material, 0.1201 bismuth oxid was obtained, equivalent to 0.1077 gm. bismuth, or 50.54 per cent. Average, 50.62 per cent. bismuth, or about 117 per cent. of the amount claimed by the formula.

SECOND EXAMINATION

Since the method previously employed by us for the determination of iodin in bismuth iodo-resorcin sulphonate had been challenged by the firm the iodin in the original specimen submitted was redetermined by several methods, which are here given in detail. The first is a modification of Elvove's method. (*Am. Jour. Pharm.*, lxxxii, 1910, 407). As carried out in this laboratory the method is as follows:

About 5 gm. of the material are heated in a 500 c.c. reflux apparatus for one hour with 25 c.c. of half-normal potassium hydroxid and 2 gm. of zinc dust. Ten c.c. of glacial acetic acid are then added, the mixture shaken and diluted with 200 c.c. of water. The mixture is then boiled for one hour in a reflux apparatus, filtered and the apparatus and filter washed with 50 c.c. of hot water. Ten c.c. of tenth-normal silver nitrate are added to the filtrate and the mixture heated for ten minutes. Fifty c.c. of diluted nitric acid are then added and the mixture boiled for five minutes, after which the precipitate is collected in a tared Gooch crucible, washed, dried and weighed with the usual precautions. The filtrate is concentrated on the water bath to about 20 c.c., diluted to 200 c.c. with water, 5 c.c. of ferric ammonium sulphate test solution added, and the excess of silver nitrate determined by titration with tenth-normal potassium sulphocyanate. The silver nitrate consumed as shown by the titration is calculated to silver iodid and the result compared with the weight of silver iodid obtained.

If no chlorid had been present in the substance tested the results obtained by the gravimetric method should have con-

formed closely to those given by the titration. Since there were discrepancies in the results obtained by the two methods the presence of chlorid was indicated and its quantity calculated. As the zinc dust used contained chlorin, suitable control determinations were carried out and the silver chlorid found deducted from the results obtained with the substance.

Results: From 0.5256 gm. of the material 0.1329 gm. silver haloid was obtained and 6.244 c.c. tenth-normal silver nitrate were consumed. Since 1 gm. silver iodid is equivalent to 42.91 c.c. tenth-normal silver nitrate and 1 gm. silver chlorid is equivalent to 70.27 c.c. tenth-normal silver nitrate the respective weights of silver iodid and silver chlorid in a mixture of the two may be determined by solving the following equation:

$$42.91\,x + 70.27\,(w - x) = c$$

In which:

w = wt. of mixed silver haloids found.
x = wt. of silver iodid in the mixture.
w − x = wt. of silver chlorid in the mixture.
c = number c.c. tenth-normal silver nitrate consumed.

Substituting the values obtained in the analysis in the above formula the equation becomes: $42.91x + 70.27\,(0.1329 - x) = 6.244$, which gives x a value of 0.113114 gm. silver iodid; this is equivalent to 0.061116 gm. iodin or 11.63 per cent.: 0.1329 gm. − 0.113114 gm. (x) = 0.019786 gm. silver chlorid: this is equivalent to 0.004891 gm. chlorin, or 0.93 per cent. From 0.5642 gm. of the material 0.1423 gm. silver haloid was obtained and 6.7 c.c. tenth-normal silver nitrate were consumed. Calculation according to the formula gives x a value of 0.120592 gm. silver iodid; this is equivalent to 0.065156 gm. iodin, or 11.55 per cent. 0.1423 gm. − 0.120592 gm. (x) = 0.021708 gm. silver chlorid, equivalent to 0.005367 gm. chlorin, or 0.95 per cent. Average, 11.59 per cent. iodin and 0.94 per cent. chlorin.

Iodin was also estimated by a modification of a method suggested by Gane and Webster for determining iodin in iodoform (*Chemical Abstracts*, iii, 1909, 1669), which is as follows:

From 0.5 gm. to 1 gm. of the material is placed in a Lintner's pressure bottle, followed by 0.200 gm. to 0.300 gm. of solid silver nitrate (previously powdered and dried for one hour at 100 C. before weighing) and 10 c.c. of 50 per cent. nitric acid. The closed bottle is then heated for six hours in a gently boiling water bath with occasional agitation. The bottle is cooled and the contents rinsed into a beaker by the use of 200 c.c. of water. About 10 c.c. of concentrated nitric acid are added and the mixture heated on the water bath for thirty minutes. The precipitate is then collected in a tared Gooch crucible, washed with 50 c.c. of hot 1 per cent. nitric acid, 15 c.c. of alcohol, followed by 5 c.c. of ether, dried and weighed

with the usual precautions. The alcohol and ether in the filtrate are removed by evaporation, the solution cooled and the unused silver salt determined by titration with tenth-normal potassium sulphocyanate, using 5 c.c. of ferric ammonium sulphate test solution as indicator. The silver nitrate consumed is calculated to silver iodid and the result compared with the weight of silver haloid obtained.

Results: From 0.5290 gm. of the material 0.1272 gm. silver haloid was obtained and 0.101214 gm. silver nitrate, equivalent to 6.0 c.c. tenth-normal silver nitrate, was consumed. Substituting these values in the formula the equation becomes, $42.91x+70.27(0.1272-x)=6$, which gives x a value of 0.107383 gm. silver iodid; this is equivalent to 0.058019 gm. iodin, or 10.97 per cent.; 0.1272 gm.—0.107383 gm. $(x)=0.019817$ gm. silver chlorid, equivalent to 0.004899 gm. chlorin, or 0.926 per cent. From 0.9425 gm. of the material 0.2271 gm. silver haloid was obtained and 0.179942 gm. silver nitrate, equivalent to 10.667 c.c. tenth-normal silver nitrate, was consumed. Calculation according to the formula gives x a value of 0.193395 gm. silver iodid; this is equivalent to 0.104491 gm. iodin, or 11.09 per cent. 0.2271 gm. — 0.193395 gm. $(x)=0.033705$ gm. silver chlorid, equivalent to 0.008333 gm. chlorin, or 0.88 per cent. Average, 11.03 per cent. iodin and 0.90 per cent. chlorin.

It should be noted that slightly lower results were obtained by this method than by the Elvove reduction method.

Iodin was also determined by the method used for the determination of this element in Anusol Hemorrhoidal Suppositories (Annual Reports of the Chemical Laboratory of the American Medical Association, ii, 1909, 34).

Results: The iodin from 0.5331 gm. of the material required 4.32 c.c. tenth normal sodium thiosulphate, equivalent to 0.054388 gm. iodin, or 10.20 per cent. The iodin from 0.1772 gm. of the material required 1.45 c.c. tenth-normal sodium thiosulphate, equivalent to 0.018256 gm. iodin, or 10.30 per cent.; average, 10.25 per cent. iodin. A third sample was fused with pure potassium hydroxid and the iodin determined as indicated above. The iodin from 0.4491 gm. of the material required 3.83 c.c. tenth-normal sodium thiosulphate, equivalent to 0.048219 gm. iodin, or 10.73 per cent.

Chlorin: The presence of chlorin in the specimen of bismuth iodo-resorcin sulphonate examined is shown by the following:

About 0.300 gm. of the material was fused with 4.0 to 5.0 gm. pure potassium hydrotid and, after cooling, the fused mass dissolved as completely as possible in warm water and the solution filtered. Sulphuric acid and solid ferric ammonium sulphate were added to the filtrate and the mixture boiled to expel iodin. The residue was cooled, diluted with water, some diluted nitric acid added, and 10 c.c. of silver nitrate test solution added. The precipitate was collected, boiled in a

reflux apparatus for several hours with a pellet of zinc and some diluted sulphuric acid. The mixture was filtered, the filtrate heated with sulphuric acid and ferric ammonium sulphate to insure absence of iodin, the mixture diluted with water and a few c.c. of silver nitrate test solution added. The precipitate was treated with diluted sulphuric acid and zinc as above described, the mixture filtered and the filtrate distilled with manganese dioxid and sulphuric acid. The vapors were collected in two Pelligot's tubes, the first containing diluted starch test solution and the second diluted solution of potassium bromid. After the distillation was completed the contents of the first tube showed no blue color (absence of iodin) and the contents of the second tube were faintly colored yellow. Addition of potassium iodid test solution to the first tube and of starch test solution to the second tube gave a decided blue coloration in each case.

Owing to lack of material chlorin was not determined quantitatively except by calculation as heretofore described.

Iodin in Potassium Iodo-Resorcin Sulphonate: This was determined by Elvove's method described above.

Results: From 0.2898 gm. of the material 0.1710 gm. silver iodid was obtained and 7.4 c.c. tenth-normal silver nitrate were consumed: 0.1710 gm. silver iodid is equivalent to 0.092391 gm. iodin, or 31.88 per cent.; 7.4 c.c. tenth-normal silver nitrate are equivalent to 0.093166 gm. iodin, or 32.15 per cent. From 0.3049 gm. of the material 0.1800 gm. silver iodid was obtained and 7.772 c.c. tenth-normal silver nitrate were consumed: 0.1800 gm. silver iodid is equivalent to 0.097254 gm. iodin, or 31.90 per cent.; 7.772 c.c. tenth-normal silver nitrate are equivalent to 0.097849 gm. iodin, or 32.09 per cent. Average of all, 32.00 per cent. iodin. Since the results obtained by weight and by titration are not widely divergent no appreciable quantity of chlorin can be present.

The iodin in potassium iodo-resorcin sulphonate was also estimated by means of the modified Gane and Webster method described above.

Results: From 0.7009 gm. of the material 0.4058 gm. silver iodid was obtained and 0.292609 gm. silver nitrate, was consumed. 0.4058 gm. silver iodid is equivalent to 0.219254 gm. iodin, or 31.28 per cent. 0.292609 gm. silver nitrate is equivalent to 0.218386 gm. iodin, or 31.16 per cent. From 0.6158 gm. of the material 0.3539 gm. silver iodid was obtained and 0.254422 gm. silver nitrate was consumed. 0.3539 gm. silver iodid is equivalent to 0.191212 gm. iodin, or 31.05 per cent. 0.254722 gm. silver nitrate is equivalent to 0.190109 gm. iodin, or 30.88 per cent. Since the results by weight and by titration are so nearly identical it is evident that no chlorin is present. The average of the results obtained is 31.10 per cent. iodin. Here, as in the bismuth salt, lower results were obtained than by the Elvove method.

Water in Potassium Iodo-Resorcin Sulphonate: This was determined by drying the material at 100 C. From 0.3898 gm. of the material a loss of 0.0407 gm. was found, equivalent to 10.44 per cent.; 0.4152 gm. of the material lost 0.0431 gm., equivalent to 10.38 per cent.; average, 10.41 per cent. loss. That this loss in weight was not due to loss of iodin was shown by determination of the iodin in the dried material, the results of which indicated that no iodin is lost at 100 C.

TABLETS OF BISMUTH, OPIUM AND PHENOL

W. A. Puckner and W. S. Hilpert

(From The Journal A. M. A., May 6, 1911, p. 1577)

Nearly three years ago,[1] a contribution from the Chemical Laboratory appeared in The Journal, dealing with the composition of tablets of bismuth, opium and phenol (carbolic acid). It was there shown that these tablets contained only from 72.65 per cent. down to as low as 12.66 per cent. of the amount of phenol stated on the label.

After publishing these results in detail and waiting a little more than two years, we again examined similar tablets of the same makes, bought in the open market. The results of this second examination were published in The Journal, Dec. 17, 1910. Instead of finding that conditions were better, that the firms had made an effort to market tablets that were true to the label, this examination showed that the phenol-content of the tablets now ranged from 63.53 per cent. down to 12.27 per cent. of the amount claimed.

This second examination also showed that the manufacturers were not sufficiently concerned with the quality of their product to call in any stock which they must have known was untruthfully labeled. In view of this fact, it was thought worth while both to learn the ages of the various tablets that were purchased at the time of, and for the purpose of, making the second examination and also to examine the most recently made tablets put out by the same firms. Accordingly, the identifying marks on each package of tablets examined and which formed the basis of the report of the second paper, were sent to the respective firms with inquiries as to the date of the manufacture of these various specimens. At the same time orders were placed in each case for the firm's most recently made product.

1. The Journal A. M. A., July 25, 1908, p. 330

The result of this work is arranged in tabulated form as follows: Table 1 gives the age of the specimens that were used for the second examination: Table 2 compares the composition of tablets as found in the first and second examinations with the composition found in the present (third) examination.

TABLE 1.—AGE OF TABLETS IN SECOND EXAMINATION

Manufacturer	Date of Manufacture	Date of Purchase	Age When Purchased
Hance Bros. & White...	Sept. 17, 1910.	Oct. 27,'10	1 month.
W. S. Merrell Chem. Co.	July 11, 1906..	Oct. 27,'10	4 years.
H. K. Mulford Co.....	Nov. 22, 1909..	Sept. 15,'10	1 year.
Parke, Davis & Co.....	Sept., 1910....	Sept. 15,'10	Under 1 mo.
Sharp & Dohme.....	June 1, 1906...	Sept. 15,'10	4 years.
F. Stearns & Co.....	August, 1906..	Oct. 27,'10	4 years.
Truax, Greene & Co....	Prior to 1906..	Sept. 16,'10	4-5 years.
H. K. Wampole & Co...	Aug. or Dec.,'08	Oct. 27,'10	2 years.
W. R. Warner & Co....	Aug. 3, 1906...	Nov. 11,'10	4 years.

TABLE 2.—COMPOSITION OF TABLETS IN FIRST, SECOND AND THIRD EXAMINATIONS

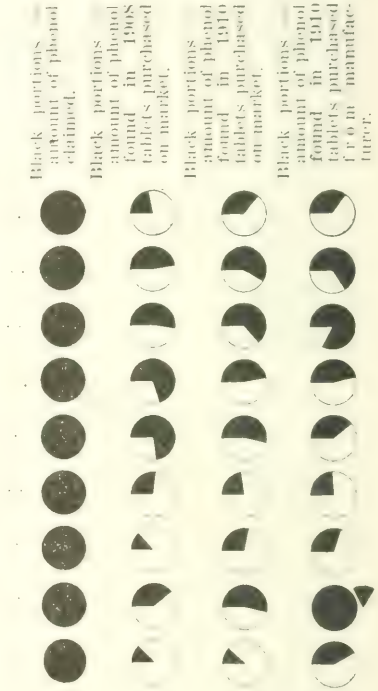
Phenol Found Expressed as Per Cent. of Amount Claimed

Manufacturer	Specimen Purchased on Market		Specimen Obtained from Manufacturer
	1908	1910	1910
Hance Bros. & White.....	21.89	34.19	34.49
W. S. Merrell Chem. Co....	48.89	57.59	68.43
H. K. Mulford Co.....	52.34	63.53	83.18
Parke, Davis & Co..... (a)	(a) 70.23		
Parke, Davis & Co..... (b)	(b) 47.02	46.86	46.83
Sharp & Dohme..... (a)	(a) 72.65		
Sharp & Dohme..... (b)	(b) 34.63	53.39	38.14
F. Stearns & Co.....	26.55	23.17	24.86
Truax, Greene & Co.....	13.69	28.09	28.24
H. K. Wampole & Co.... (a)	(a) 46.14		
H. K. Wampole & Co.... (b)	(b) 39.31	53.75	112.64
W. R. Warner & Co.....	12.66	12.27	41.47

Strange as it may seem, some of the manufacturers wrote as if they had not known of the former publication of the laboratory's examination.

Wm. R. Warner & Co. writes that it is going to engage the services of a commercial chemist to examine the stock and that it will not offer the tablets for sale until assurance is had that the tablets are true to claim. While it may cause some surprise to learn that this firm must engage outside

talent to learn the quality of its own wares, the decision to discontinue the sale of its practically worthless stock is to be commended.



The above presents the findings of the Association chemists in a graphic form and shows the great discrepancies between the claims made for the tablets and the actual facts. The solid black portions represent the phenol-content. In the first column is given the phenol-content claimed by the manufacturer; in the second column is shown the actual phenol-content found in the tablets purchased in 1908; the third column represents the phenol-content as found in the tablets purchased on the market in 1910, while the fourth column shows the phenol-content of the tablets purchased in 1910 direct from the manufacturer. Note the excess of phenol in the tablets sent by H. K. Wampole & Co. in filling the order for a bottle of the most recently made products.

The tablets which were obtained direct from H. K. Wampole & Co. and which were found to contain an amount of phenol in excess of the amount claimed were quite different in appearance when received from any previously examined in

that they were damp and had a strong odor of phenol. About two months later, the tablets of this batch which remained in the bottle presented a most remarkable appearance in that they were covered with an efflorescence of crystals of phenol. Should these tablets be dispensed on a physician's prescription the possibilities are that the pure phenol would come in direct contact with the tongue and throat and produce painful burns. Of course these tablets are quite unfit for use.

Another important matter brought out is the fact that ready-made mixtures, such as these tablets, may be four or five years old before they leave the hands of the wholesaler. While, in this case, the efficiency of the remedy is not influenced by age, it is a well-known fact that many drugs rapidly deteriorate. If tablets such as these are likely to be four or five years old before they leave the wholesale house, how old will they be before they are dispensed on a physician's prescription? This question is a pertinent one and the answer which the laboratory's work furnishes—should go much to discourage the prescribing of such ready-made mixtures.

UNRELIABLE PHARMACEUTICAL PRODUCTS

(*From The Journal A. M. A., May 6, 1911, p. 1435*)

The Following Editorial Comment Was Made by The Journal A. M. A. on the Above Contribution

For some years past, pharmaceutical houses have put out in tablet form an enormous number of combinations of drugs of real or fancied value. In many instances the combinations are not suited to the tablet form and it is not surprising that many of these tablets do not conform to the composition that is claimed for them. It is not to be inferred that the manufacturers wilfully put up products that are false to label, but rather that many of the combinations are pharmaceutically impossible. That is to say, it is pharmaceutically impossible—or at least, commercially impracticable—to manufacture, in tablet form, some of the combinations that are listed in the manufacturers' catalogues.

These tablet-combinations have been offered to the medical profession primarily because such products are considered as "business-getters" and the manufacturers seem to have tried to outvie one another in the number of combinations which they offer physicians. In most cases these tablets have been made, not to supply, but to create a demand, and as soon as

one manufacturer has put out a new combination, his competitors immediately put similar combinations on the market. The result has been harmful to medicine and a discredit to pharmacy.

With the object of showing how pharmaceutically impossible it is to make some of these tablet-combinations, our chemists were asked to examine some of the several brands of tablets said to contain bismuth subnitrate, opium and phenol (carbolic acid). While this tablet is, in itself, of comparatively little importance, it was selected as a type because practically all pharmaceutical houses offer it for sale, because its manufacture offers some difficulties and because its phenol-content can be accurately determined. More than two years ago, the leading brands of these tablets were bought in open market, analyzed by the Association's chemists and the results published in THE JOURNAL.[1] Two years later, similar products of the same firms were again purchased, analyzed and the results published.[2] Both of these reports showed that the composition of the tablets examined—at least so far as their phenol-content was concerned—could not be relied on. The second examination brought out the further fact that practically all the manufacturers whose products had been examined had apparently made no effort either to modify the claims on the labels, to improve the quality of the tablets or to withdraw the product from the market.

In the "Propaganda for Reform" department of this issue appears the third, and final, article from our chemical laboratory on this subject. It will be found not only to verify the statements of the previous two articles, but also to bring out another point that is of almost as great importance as the unreliability in composition, namely, that ready-made mixtures of this type are more than likely to be several years old before they reach the physician. While this does not, of necessity, impair the efficiency of all drugs, it must in many instances be detrimental to scientific prescribing.

The three exhaustive and painstaking examinations made in the Association's laboratory and the articles that are based on these examinations teach some valuable lessons, both specifically and generally. Specifically, they show that there are probably no tablets of bismuth, opium and phenol on the market which contain the amount of phenol stated on the label; this, too, even though the tablets are obtained direct

1. July 25, 1908, p. 330.
2. Dec. 17, 1910, p. 2169

from the manufacturer. It is true that in one case the tablets obtained direct from the manufacturer contained not only all the phenol claimed, but a very appreciable percentage in excess of that amount. These tablets, however, bore such evident marks of having been "made to order" that the general findings of the laboratory were in no way vitiated. Essentially then, it has been proved that it is impracticable, if not impossible, to manufacture tablets of bismuth, opium and phenol so that the phenol-content can be relied on.

Generally, the results are of even greater importance. First is the very evident unwisdom of attempting the pharmaceutically impossible merely for the sake of achieving pharmaceutical "elegance." When one considers the enormous number of tablet combinations on the market—some firms listing over a thousand—and further realizes that undoubtedly in a great number of cases such combinations are absolutely worthless so far as accuracy of dosage is concerned, the menace that such forms of medication must be to scientific medicine becomes apparent.

Second is the responsibility that rests on the pharmaceutical manufacturer for the deplorable conditions that these investigations have exposed. Physicians naturally have supposed that they could rely on the statements of such pharmaceutical firms as those whose products are affected in this exposure, at least so far as the composition of non-proprietary preparations is concerned. The defections are those of the manufacturing pharmacists. It is no excuse for them to say that they are but supplying a demand when they put out such products. The physician, of necessity, does not always realize the limitations to the art of compounding drugs and it has long been considered the function of the pharmacist to enlighten him on such technical points. In the present instance, however, the physician, instead of being advised, has been taken advantage of. Further, as has already been stated, the manufacturers are not so much supplying a demand as attempting to create a demand. Moreover, if they wish to retain the confidence of physicians they should frankly admit, when asked to put up combinations that are not pharmaceutically practicable, that it cannot be done. Instead of taking this attitude, they seem to have decided that, so long as there is money in pretending to make tablets that cannot be made, they might as well get what financial benefit they could out of the pretense.

In view of the facts brought out by our chemists, we are justified in asking a question: We know that the products

examined were untrue to label when first taken up over two years ago; we know, further, that the same class of products were equally unreliable two years later, when examined the second time; we also know that still more recently these tablets, even when purchased direct from the manufacturer, are not to be depended on. Twice THE JOURNAL has given publicity to the unreliability of these products, but the manufacturers have neither profited by it nor apparently paid any attention to it. Now, for the third time, attention is directed to the same conditions. We are justified in asking therefore: Will reputable pharmaceutical houses continue to put on the market products which they know to be not only unscientific but actually fraudulent, simply because it is "business?" The medical profession awaits the answer.

CHICHESTER'S DIAMOND BRAND PILLS

(Reprinted, with additions, from The Journal A. M. A., May 27, 1911, p. 1591)

A preparation known as "Chichester's Diamond Brand Pills" is, and has been for years, extensively advertised in newspapers, drug journals, etc. While in these advertisements nothing is said regarding the therapeutic uses of the preparation, the public to a large extent, knows it and buys it as an abortifacient remedy. This is shown by letters which THE JOURNAL receives of which the following is an example:

"If it is possible would you kindly give me the ingredients of Chichester's Diamond Brand Pills? They are sold to produce abortion and are guaranteed under the Food and Drugs Act, the serial number being 1867.

A trade package, "large size," of Chichester's Diamond Brand Pills was purchased on the open market and examined with especial reference to the presence of commonly reputed abortifacient drugs. The pills were put up in a small tin box, "elegantly and artistically decorated in red, black and gold," "air, dust and moisture proof, with hinged lid," on which is printed:

"Distributed by Chichester Chemical Co."

The package contained twenty pills and considerable advertising matter, wrappings, etc. Attention is called to some of the statements in a booklet contained in the package entitled:

"Relief for Ladies. Directions for Use of Chichester's Diamond Brand Pills."

"To Our Old Customers.

"Change of Name

"Our Remedy was formerly called 'Chichester's English Pennyroyal Pills,' but on account of unscrupulous imitations offered under the name of 'pennyroyal' our remedy will hereafter be known only as 'Chichester's Diamond Brand Pills.' "

"Treatment may be begun at any time, although in some instances the pills are more effective if taken about the regular time for the menstrual flow. As a rule, however, it is found that more satisfactory results are secured by beginning treatment at once and continuing it until the pills give relief."

Only one small page each is devoted to "Amenorrhea," "Dysmenorrhea" and "Directions," the remainder is taken up with testimonials, cautions to "Take no other," "Refuse all others," "Beware of imitations," etc.

EXAMINATION

The aggregate weight of the pills contained in the package amounted to 8.7963 gm., or about 0.44 gm. for each pill. The pills, when deprived of their coatings, weigh about 0.2600 gm. (4 grains) each, this coating constituting nearly half their original weight. The coatings consist essentially of calcium carbonate, although a small quantity of sugar is present.

By the usual tests the presence of some preparation of aloes and of ferrous sulphate was demonstrated. Tests for the presence of black hellebore, tansy pennyroyal, savin and certain other reputed abortifacients resulted, in each case, negatively. Ergot or its preparations could not be detected. While the identification of mixed plant extracts, especially those which contain constituents not readily isolated, is a matter of great difficulty and is often impossible, it would appear, from the examination, that the chief medicinal constituents of the pills are aloes and iron sulphate, the latter ingredient being present to the extent of about ½ grain to each pill. The statement of the manufacturer that the pills are sugar coated is scarcely warranted by the facts. The change of name from "Chichester's English Pennyroyal Pills" to one in which the word *"Pennyroyal"* does not occur is significant in view of the fact that no pennyroyal could be found in the pills. Under the Food and Drugs Act it would be illegal to sell as "Pennyroyal Pills," pills that did not contain that constituent.

A package of these pills retails for $2, or at the rate of 10 cents for each pill. An examination of the price lists of several large manufacturers of pharmaceuticals reveals that pills very nearly corresponding to the above may be bought in quantities for about 22 cents per hundred. The profits in

retailing at $10 per hundred ought to be satisfying even to the most avaricious.

THE JOURNAL commented editorially on the above report as follows:

"The above calls attention to a vicious state of affairs—the selling to the public of drugs of reputed abortifacient properties. We believe there is not a state in the Union which has not adopted laws against it, but in spite of this, these preparations, in thin disguise, are shamelessly advertised in newspapers and as shamelessly and boldly sold over the counters of many drug stores. While it is true that many of these nostrums are merely fraudulent, rather than dangerous, yet not a few contain potent and—for the purpose for which sold—villainous drugs.

"As shown by our chemists, Chichester's Diamond Brand Pills seem to be simply the old aloes and iron sulphate pills with slight modification. While these pills were sold originally as "pennyroyal" pills, the Food and Drugs Act, which forbids lying on labels, has apparently compelled the manufacturers to omit the word "pennyroyal."

BEFORE AFTER

Photographic reproductions (reduced) of advertisements of Chichester Pills before and after the passage of the Food and Drugs Act. The Association chemists found no pennyroyal in these pills and under the pure food law it would be illegal to call them "Pennyroyal Pills." Was this responsible for the change in name?

"Since it is well known that there is no drug or combination of drugs which, taken by the mouth, will with certainty produce abortion, it is not probable, to judge from the constituents found in these pills, that they would produce the result desired by the purchaser. Nevertheless, the use of this nostrum is pernicious and in the interest of public health and public morals its sale, and the sale of similar nostrums, should be prohibited."

Details of Analysis

The pills were weighed separately from the wrappings and circulars. The weight of the pills from an entire box (twenty) amounted to 8.7963 gm. or 0.4398 gm. for each pill.

Qualitative tests indicated that the coatings of the pill consist essentially of calcium carbonate and sugar, the latter substance being present in very small amounts. Further qualitative tests on the water-soluble portion of an entire pill indicated the presence of iron, chiefly in the ferrous condition, and of sulphate, both constituents being present in appreciable amounts. An entire pill was weighed, its coating carefully removed and the residual portion again weighed. The coated pill weighed 0.4468 gm.; with its coating removed its weight was 0.2607 gm. or 58.3 per cent. of the original.

Aloes.—On crushing one of the pills in a mortar an odor like aloes was noticed. The powder was extracted with hot water and the cooled filtrate treated with a concentrated solution of sodium borate. After standing a few minutes a greenish fluorescence resulted.

Ash.—An entire pill was ashed in a porcelain dish at a low red heat and the residue weighed. One pill, weighing 0.4564 gm., gave an ash of 0.1231 gm., or 26.9 per cent. Qualitative tests indicated that the ash consists essentially of calcium carbonate and iron oxid.

Iron.—The ash from one pill was dissolved as completely as possible in dilute hydrochloric acid, sufficient nitric acid added and the solution evaporated to small bulk. The solution was diluted with water, filtered and ammonia water added to slight excess. The precipitated ferric hydroxid was collected in a weighed Gooch crucible, dried, heated to redness and weighed as ferric oxid; 0.1231 gm. ash (equivalent to 0.4564 gm. pill substance) gave 0.0163 gm. ferric oxid equivalent to 0.03097 gm. anhydrous ferrous sulphate ($FeSO_4$) or 6.79 per cent.

Sulphate.—Five pills (2.1880 gm.) were dissolved, in hydrochloric acid as completely as possible, filtered and the filtrate made up to 200 c.c. From 100 c.c. of this solution the sulphate was precipitated by means of barium chlorid, the precipitate collected, dried, ignited and weighed as barium sulphate; 100 c.c. of the above-mentioned solution (representing 1.094 gm. of the material) gave 0.1277 gm. barium sulphate equivalent to 0.0831 gm. ferrous sulphate ($FeSO_4$) or 7.43 per cent.

Volatile Oils.—Five pills were placed in a steam distillation apparatus and 50 c.c. water added. The mixture was allowed to stand 12 hours, and was then distilled with steam for one hour. The distillate had no odor of tansy, savin or pennyroyal, and this was taken to indicate that these substances were absent.

Resins.—One hundred c.c. of an alcoholic extract from the pills (representing 0.391 gm. pill mass) were evaporated to small bulk and the residue poured into a large excess of water. The merest trace of precipitate was formed on standing. This trace of precipitate was collected, dissolved in alcohol, the solution evaporated, the residue dried at 98 C. and weighed. No weighable residue was obtained. Preparations of cimicifuga, jalap or podophyllum cannot be present in more than the merest traces.

Alkaloids.—An acid, hydro-alcoholic solution of the pills was prepared by treating a quantity of the pill mass successively with alcohol, water and diluted acetic acid and mixing the respective filtrates. The mixture was evaporated to a thin syrup, taken up with water and shaken out with chloroform-ether mixture from acid solution. The residue obtained by evaporation of the solvent was taken up with acidulated water and filtered. The filtrate gave no characteristic reactions when treated with the usual alkaloidal reagents. The acid solution remaining after shaking out with ether-chloroform, was rendered alkaline by ammonia water and shaken out with the above mentioned solvent. The ether-chloroform was drawn off, washed with water and shaken out with diluted hydrochloric acid. The acid solution was made alkaline and shaken out with fresh portions of the ether-chloroform mixture. The solvent was evaporated, the residue taken up with acidulated water, filtered and portions of the filtrate treated with iodin test solution and with mercuric potassium iodid test solution. No precipitation was obtained in either case.

Microscopic Examination.—The insoluble residue remaining after treatment of the crushed pills successively with alcohol, water and acetic acid, was examined under the microscope. Considerable amorphous, black material was observed which was not positively identified. A small quantity of vegetable tissue, evidently glycyrrhiza, was present.

DRIED MAGNESIUM SULPHATE

W. A. Puckner and L. E. Warren

(Reprinted from the American Journal of Pharmacy, June, 1911)

The committee of the American Pharmaceutical Association for standards of unofficial drugs and chemical products having considered "dried magnesium sulphate" the subject was assigned to the senior author of this paper as referee for the preparation of tentative standards. Accordingly provisional academic standards for the substance were prepared and submitted for criticism to a number of manufacturers of chemicals and to several chemists whom it was thought would be interested. At the same time several brands of the product were purchased and examined.

Dried magnesium sulphate is official in several of the foreign pharmacopeias. In the Pharmacopeia formerly official in Austria the method directed for the preparation of the product was to dry the crystallized magnesium sulphate first on the water bath with stirring and then on a sand bath until a loss of 43 per cent. should be attained. The composition of the residual salt was supposed to correspond approximately to the formula $MgSO_4 + H_2O$. Such a salt should contain about 87.0 per cent of anhydrous magnesium sulphate. In the last edition of the Austrian Pharmacopeia it is directed to dry the salt on the water bath at 100 C. with stirring until 36 per cent. of the original weight has been lost. The formula of such a salt should be approximately $MgSO_4 + 2H_2O$, corresponding to about 77.0 per cent. anhydrous magnesium sulphate. The directions given by the German Pharmacopeia (Ed. 5) are to dry the salt in a porcelain dish on a water bath until it has lost from 35 to 37 per cent. of its weight. Such a salt should contain from 75.15 per cent. to 77.54 per cent. of anhydrous magnesium sulphate ($MgSO_4$) yet the purity rubric demanded by this same authority is only 70 per cent. of anhydrous substance. The salt is also official in the Swiss Pharmacopeia, the method of preparation being similar to that prescribed in the German Pharmacopeia except that the crystallized salt is allowed to effloresce in the air before heating.

Dried magnesium sulphate was prepared by several methods. The first was by the method prescribed in the German Pharmacopeia. This consists in drying the crystallized salt on the water bath with stirring until the substance has lost from 35 to 37 per cent. of the original weight. Owing to the time

required it was found impracticable to dry the crystallized salt on the water bath until the specified loss had occurred. A specimen of 50 gm. of the commercial salt was dried in this manner during several working days and the loss amounted to but 33.7 per cent. instead of a minimum of 35.0 per cent. A duplicate lost 33.8 per cent. in 45 hours drying. Magnesium sulphate was determined in this specimen and 75.2 per cent. of the anhydrous salt found. When dried at 100 C. in the air oven for four hours a loss of 3.4 per cent. was noted in the same specimen.

Dried magnesium sulphate was also prepared by heating 100 gm. of crystallized magnesium sulphate in an air oven, first at a temperature of 60-70 C. and then at a gradually rising temperature until the specimen practically ceased to lose weight. A loss of 41.2 per cent. was noted. Several days' heating at a temperature of 100 C. with occasional maxima of 110 C. failed to secure a loss of 43 per cent. as required by the former Austrian Pharmacopeia (corresponding to the formula $MgSO_4.H_2O$). This specimen contained 84.7 per cent. anhydrous magnesium sulphate.

The most satisfactory method of preparation was found to be to dry the crystallized salt at a temperature of 60-70 C. with stirring and finally at 100 C. until a loss of 37 to 40 per cent. had been obtained. A specimen so prepared which had been dried until 39.9 per cent. of the original weight had been lost contained 81.9 per cent. of anhydrous magnesium sulphate.

Three specimens of dried magnesium sulphate bearing the labels of as many makers were purchased on the open market and examined with reference to their content of anhydrous magnesium sulphate and to their loss when dried at 100 C. Apparently as a protection against moisture all of the specimens purchased had been wrapped in paper before being packed in the containers. Two of the latter were composed of thick pasteboard and the other of tin with a close fitting cover.

The magnesium, both in the laboratory specimens as prepared and in the specimens as purchased, was weighed as magnesium pyrophosphate, the method being described in detail in another part of this paper. It was found that constant weight could not be attained when drying the commercial salt at 100 C. (at least during no reasonable length of time), the specimens continuing to lose weight very slowly even when dried for several days. It was therefore found expedient to record the results after drying for four hours at 100 C.

The specimen bearing the label of the Mallinckrodt Chemical Works contained 67.2 per cent. anhydrous magnesium sulphate

and lost 7.3 per cent. of water. The Powers-Weightman-Rosengarten specimen contained 64.9 per cent. anhydrous magnesium sulphate and lost 19.4 per cent. on drying. The Merck specimen contained 54.3 per cent. anhydrous magnesium sulphate and lost 26.1 per cent. on drying. While no claim for purity or strength is made on the label of this specimen, the product sold by this firm is described in Merck's Index (1907) as containing about 2 molecules of water, corresponding to about 77.0 per cent. of anhydrous magnesium sulphate. The product as actually sold, therefore, contains but about 70.5 per cent. of the amount of anhydrous magnesium sulphate claimed for it. The result obtained for all the specimens examined are tabulated below:

Laboratory Number or Brand	Anhydrous Magnesium Sulphate ($MgSO_4$)	Water Lost in Four Hours at 100°C.
1	75.26	3.4
2	84.68	Not determined
3	81.0	Not determined
U. S. P.	67.26	7.29
P. W. R.	64.87	19.42
Merck	54.27	26.16

Tests for heavy metals and for arsenic were made on all of the specimens examined by methods described in another portion of this paper. The result in each case was negative.

The assertion is made in the literature that dried magnesium sulphate absorbs moisture when exposed to the air and thus tends to revert toward the crystalline condition. As the crystalline salt is markedly efflorescent when exposed to the air (even losing as much as 7 to 8 per cent. of its weight) it seemed worth while to determine how far the dried salt would absorb moisture. Accordingly a specimen which had lost 41.2 per cent. of the original weight during the process of manufacture was exposed in a flat-bottomed dish in a place protected from dust and a flat-bottomed dish containing water was placed beside it. The water was replenished from time to time as it evaporated and the increase in weight of the exposed salt noted. In two months the specimen, originally weighing 5.0027 gm., had gained 1.813 gm., equivalent to 36.24 per cent. of the original weight.

The examination shows that the dried magnesium sulphate on the American market is far from uniform in composition. This condition might be explained from the lack of authorita-

tive standards for the product in this country. Since magnesium sulphate is usually administered in solution and since the dried salt contains only about 50 per cent. more of real magnesium sulphate ($MgSO_4$) than the official crystallized one it would appear that the dried salt is superfluous. Probably for these reasons the manufacturers have not considered the substance of sufficient importance to subject its manufacture to proper laboratory control.

Based on the provisional academic standards as first prepared but modified as found necessary by the results of the experimental work, and by the suggestions offered by those to whom the provisional description was submitted for criticism, the following standards for dried magnesium sulphate are suggested:

Dried Magnesium Sulphate—Magnesii Sulphas Exiccatus. Magnesium Sulphate dried at 100 C. (212 F.) corresponding to from 77.5 to 81.5 per cent. absolute magnesium sulphate.

Dried magnesium sulphate may be prepared by heating (with stirring) 100 parts of crystallized magnesium sulphate in a tared porcelain dish in a drying oven first at a temperature of 60 C. to 70 C. (140 F. to 158 F.) and then at a gradually rising temperature until the substance has lost from 37 to 40 per cent. of its weight.

A fine white powder, without odor, and having a cooling, saline, bitter taste. It is almost completely soluble in water. When exposed to air it absorbs moisture.

An aqueous solution of the salt (1 in 40) should be neutral to litmus paper.

When mixed with ammonium chlorid test solution and ammonia water, the aqueous solution of the salt (1 in 40) yields with sodium phosphate test solution, a white crystalline precipitate. With barium chlorid test solution the aqueous solution of the salt yields a white precipitate insoluble in hydrochloric acid.

Ten c.c. of the aqueous solution of the salt (1 in 200) should not respond to the time limit test for heavy metals prescribed in the United States Pharmacopeia, 8th Revision. Five c.c. of the aqueous solution of the salt (1 in 40) should not respond to the modified Gutzeit's test for arsenic, United States Pharmacopeia, 8th Revision.

If from 0.200 gm. to 0.300 gm. of dried magnesium sulphate be dissolved in 50 c.c. of water, the solution filtered if necessary and if 10 c.c. of ammonium chlorid test solution, 10 c.c. of sodium phosphate test solution

* Our thanks are due to those manufacturers and chemists who have made suggestions and criticisms in the preparation of the provisional standards for dried magnesium sulphate.

and sufficient ammonia water to render the mixture alkaline, be added in the order named, shaking after the addition of each reagent, the mixture allowed to stand for twelve hours, the precipitate collected in a tared Gooch crucible, washed with 1 per cent. ammonia water until free from chlorids, dried, heated to low redness for 15 minutes, cooled and weighed, the weight of the resultant magnesium pyrophosphate should correspond to at least 77.5 per cent. of pure anhydrous magnesium sulphate ($MgSO_4$).

PIX CRESOL

W. A. Puckner and W. S. Hilpert

(Reprinted, with additions, from The Journal A. M. A., June 10, 1911, p. 1788.)

In a paper on "The Abuse of Chemical Formulas" several examples were given of the various methods employed by "patent medicine" concerns to give standing to their products by assigning to them a chemical formula. In some cases the formulas given are impossible, in other cases they may represent the chemical composition of only one constituent or it may be an attempt at both. To a chemist such formulas are absurd and on seeing a formula which he knows to be wrong he naturally thinks "Fake," "Ignorance," or both. Just such a formula ($C_{11}H_{11}NSO$) applied to a product called Pix Cresol, manufactured by the "Pix Cresol Chemical Co., Kansas City, Mo.," attracted our attention. No mention of such a formula can be found in such works as Richter's most complete Index of Carbon Compounds, nor the three supplemental volumes published, 1901-1905, by the German Chemical Society and Beilstein's Organic Chemistry (3rd Edit.). This fact, supplemented by inquiries from correspondents as to the composition of the substance made it seem worth while to make a chemical examination of it.

The examination was made and showed that the essential constituent was oxyquinolin sulphate. As potassium sulphate was also found it was concluded that Pix Cresol was a preparation containing a mixture of oxyquinolin sulphate and potassium sulphate, which has also been known in the past under the proprietary name, "Chinosol." At this time a letter was referred to the laboratory containing the report of an analysis of Pix Cresol, which showed the presence of oxyquino-

1. Puckner, W. A.: Report of the Chemical Laboratory of the American Medical Association, iii, 7.

lin sulphate but no potassium sulphate. As this indicated that Pix Cresol contained as its essential constituent the substance now sold as Chinosol, the laboratory purchased a new specimen of Pix Cresol from the Chicago representatives of the Pix Cresol Co. The examination of this specimen showed that it consisted of approximately 21 per cent. oxyquinolin sulphate, about 8.3 per cent. potassium sulphate and the remainder almost entirely milk sugar.

It is evident, then, that both the specimen of Pix Cresol obtained directly from the manufacturers and also the one purchased more recently from the Chicago agent, contain as an essential constituent Chinosol of the composition sold formerly. The substance now sold under the name Chinosol and described in New and Nonofficial Remedies is pure oxyquinolin sulphate, and as the exploiters of Pix Cresol probably obtain their supply of oxyquinolin sulphate from the Chinosol Company, the sole American agents for Chinosol, it is to be expected that Pix Cresol should change in composition. It is probable that the analysis referred to the laboratory deals with a more recent specimen than the two examined in the Association laboratory.

Analytical Details

The characteristic color, odor and taste of Pix Cresol suggested the presence of oxyquinolin sulphate as an essential constituent. Its presence was established by the following tests made on the aqueous solution of Pix Cresol: Ferric chlorid solution produced a green color when added to the solution; copper sulphate yielded a yellow precipitate; barium chlorid yielded a white precipitate; sodium carbonate yielded a white precipitate, which was sparingly soluble in water, more readily in alcohol, and when washed and dried melted at from 72 C. to 73 C., the melting point of 8-hydroxyquinolin. The identity of this substance was further established by the following tests: It dissolved in alcohol to a colorless solution which became yellow on the addition of water; dissolved in water it gave a brownish-red color on the addition of ferrous sulphate, and a green color with ferric chlorid solution.

Ignition of Pix Cresol yielded a white residue soluble in water and responding to tests which indicated the presence of potassium and sulphate and the absence of other metals. On heating, Pix Cresol turned dark and finally charred, yielding an odor at first phenol-like and then like burning sugar. On treating the substance with absolute alcohol a yellow solution resulted leaving a white residue soluble in water and which responded to tests for potassium, sulphate and milk-

sugar. The following tests were relied on to identify milk-sugar as a constituent of this residue: It reduced Fehling's solution, but did not reduce a solution of copper acetate acidified with acetic acid: on dissolving in concentrated nitric acid, boiling the solution and then allowing to cool slowly, white crystals appeared, which under the microscope had the same shape as mucic acid crystals obtained by similar treatment of pure milk-sugar: placed in contact with concentrated sulphuric acid no darkening or charring took place: when heated it yielded an odor of burning sugar: it was rather slowly soluble in water.

Quantitative estimations of nitrogen, sulphate and potassium were made. The Kjeldahl nitrogen method was used, yielding the following results:

Sample Wt. in Gms.	N/10 Acid Required	Weight of Nitrogen	Per Cent. Nitrogen
1.3843	14.70	0.02048	1.48
1.3816	15.40	0.02144	1.56

The average of these estimations, 1.52 per cent. nitrogen, is equivalent to 21.14 per cent. oxyquinolin sulphate ($C_9H_7NO)_2.H_2SO_4$.

Determining the total sulphate as barium sulphate in the usual way the following results were obtained:

Sample Wt. in Gms.	Barium Sulphate Weighed	Per Cent. SO
0.6993	0.1675	8.22
0.6954	0.1684	8.15

The potassium was estimated and weighed as the chlorplatinate with the following results:

Sample Wt. in Gms.	Weight of Chlorplatinat	Equivalent of Potassium Sulphate	Per Cent. Potassium Sulphate
0.4018	0.0935	0.0336	8.35
0.3851	0.0888	0.0318	8.27

The average of these results, 8.31 per cent. potassium sulphate, was subtracted from the total sulphate content converted to potassium sulphate, leaving a quantity 9.5 per cent. potassium sulphate, the sulphate content of which is equivalent to 20.99 per cent. oxyquinolin sulphate $(C_9H_7NO)_2.H_2SO_4$. This figure agrees with the oxyquinolin sulphate content calculated from the nitrogen found, viz., 21.14 per cent., making an average of 21.06 per cent.

From these results it was assumed that Pix Cresol consisted essentially of oxyquinolin sulphate 21.06 per cent., potassium sulphate 8.31 per cent. and the remaining 70.63 per cent. almost entirely milk-sugar.

EDITORIAL NOTE: In view of the Council on Pharmacy and Chemistry's findings, viz., that chinosol is a powerful antiseptic but a feeble germicide and considering that Pix Cresol contains but 21 per cent. oxyquinolin sulphate, the absurdity of the following claims made for Pix Cresol require no further comment:

"Pix Cresol is an Absolutely Sure and Yet Perfectly Safe, Never Failing Destroyer of Pus (*Staph. Pyogenes Aureus.*)"
"It is germicidal, bactericidal, bacillicidal. It is certain as a microorganism destroyer. It destroys absolutely."
"Ridding the blood of germs, it aids in rendering it replete with oxygen."
"It kills the germs."
"No organism that is causative of morbid processes can withstand it."
"It destroys microorganisms of all kinds. It destroys them absolutely."
"The germ's tenacity of life does not avail against its action as germicide."
"It destroys the spores and toxins utterly."

A further estimate of the pseudo-chemical company, bearing the name of this "strongest, safest, least expensive medical antiseptic, disinfectant and deodorizer known" may be gained by a cursory glance at some of its "specialties":

"Maizinin compound, Positive Chill and Malaria Specific" the firm says, "prepares the parasites for execution by the leukocytes." It is said to contain arsenic, while the name implies the presence of some plant drug.

"Psora, the Syphilis Specific," is a shot-gun mixture said to be "the scientific combination of the soluble Triple Iodids with the active principles of Echinacea, Cascara amagra, Berberis aquif., and Phytolacca rad.," and is claimed to make "the syphilitic lesions disappear and fail to return."

"Rectoids—Cones for the treatment of all rectal trouble," are said to be "a combination of Rectin (Pix) compounded from Buckeye, Collinsonia, Hammamelis, Belladona, Pix Cresol."

"Tablets for the Female—Pix Cresol Uterettes," it is said, "for sanitary purposes may be continued forever . . ."

When one realizes that this sort of pseudo-scientific twaddle is accepted by many physicians at its face value, the outlook for therapeutics seems dark, indeed. So long as the existence of such concerns is tolerated by the medical profession, so long will there be a crying need for a "Propaganda for Reform in Proprietary Medicines."

2. Council on Pharmacy and Chemistry Reports, 1910, p. 47.

LIQUID LIFE

W. A. Puckner and L. E. Warren

(Reprinted, with additions, from The Journal A. M. A., Aug. 5, 1911, p. 405)

A physician wrote to THE JOURNAL that for six years one of his patients had been taking about fifty bottles annually of a preparation called "Liquid Life:" he requested information concerning the composition of the remedy. The inquiry was referred to the Association's laboratory.

The price of the preparation being 75 cents for each bottle, it seemed a pity that patients like this one should continue to be separated from their money by a nostrum which, from its name and descriptive circulars, appeared to be a sham. Hence it was explained to the correspondent that if he would send an original package of the preparation to the Association's laboratory a cursory examination would be made sufficient in all probability to show his patient the folly of her faith in the nostrum.

An original package of "Liquid Life" having been received, a cursory examination of it was made, which showed that the preparation is essentially an aqueous solution of Epsom salt, containing some Glauber's salt, the mixture being sweetened with saccharin. The facts brought out by the cursory examination having shown that the preparation is an outrageous imposition on the public, it was decided to make a more complete investigation with the view of publishing the results.

On the label of "Liquid Life" the nostrum is described in part as follows (the spelling and diction being exactly transcribed):

"LIQUID LIFE
A
TRUE ANTITOXINE

This antitoxine is non-poisonous and non-alcoholic. It will expel all alcohol from the system at once, and so requires a great deal more antitoxine and time to effect a cure if any alcohol is used while taking it, but you can use whatever tobacco you have been accustomed to."

ARRESTS DISEASES AND PREVENTS THE DEVELOPMENT OF GERMS

"All contagious diseases are germ diseases, and manifest themselves first as headache, pain in the back, lassitude and rise of temperature, at this stage a few doses of the antitoxine will arrest them at once and prevent any further development of the germs, no matter what their nature may be."

THE PATIENT SHOULDN'T MEDDLE WITH THE LEUCOCYTES!

"It is important that their should be no interference with the action of the leucocytes or white corpuscles by using purgatives or drugs of any kind while taking the antitoxine. If the bowels move very freely at first they will check them later, and if they do not move, wait till they do."

A paragraph taken from the circular describing "Liquid Life" is given herewith. Considering its length, it is sub-

mitted as probably being the most faulty in diction, the most replete in false statements and the most barren of truthful suggestions of any paragraph in "patent medicine" literature.

"THE HOME PHYSICIAN
WHY LIQUID LIFE MAKES ONE.

First, it is antitoxine to all contagious diseases and so removes the fear of infection from the family. If given early, acts as a preventive, given later subdues the disease; is non-poisonous and non-alcoholic; there are no reactions or bad effects from it no matter how long it is taken. It contains in itself everything with the exception of food that should be taken into the stomach to keep the family in perfect health. Children born under the influence of the antitoxine, are just splendid and remain so after birth and grow up symmetrical with a healthy body and a clear brain, for when a dose of the antitoxine is given you call into action not only one physician but millions (the Leycocties) and every one of them is a supernal surgeon and their power to restore the body to health is supreme, even in those diseases that have been found difficult to cure before, such as Pneumonia, Catarrh, Appendicitis, Blood Poison from any cause, Syphilis, Cancer, Malignant Diptheria, Erysipelas, Scrofula, Tetanus or Lockjaw, Consumption, all Fevers, Rheumatism, Womb diseases, Bright's Disease, Diabetes and other diseases called incurable. Ladies will find the antitoxine is all they require to keep themselves in perfect health, and if taken for a short time before confinement will relieve them of half the pain and danger. It can also be used externally with marvelous effect in all cases requiring outside applications, or injected into all the orifices of the body where there is disease, in fact, being a true antitoxine, it solves the problem of Health and Disease."

To those conversant with the principles of medicine the reading of the label and circulars would alone be sufficient to condemn the nostrum as a humbug. Others might, however, be impressed as strongly by this jumble of meaningless phrases and vicious misrepresentations as by a logical and truthful statement of facts.

The labels indicate that "Liquid Life" is manufactured by the T. B. Chemical Co., Newark, N. J. The preparation is a pale yellow, faintly fluorescent liquid, having a faint peppermint-like odor and a harsh, disagreeable taste. The presence of magnesium, sodium, a sulphate and small amounts each of saccharin, zinc and quinin was demonstrated by the usual tests. Ammonium salts were absent. The absence of cocain, morphin and their derivatives and substitutes was shown.

Quantitative determinations indicated that the composition of "Liquid Life" is essentially as follows:

Crystallized quinin sulphate	0.0566 gm.	in 100 c.c.
" zinc sulphate	0.2416 gm.	in 100 c.c.
" magnesium sulphate (Epsom salt)	13.34 gm.	in 100 c.c.
" sodium sulphate (Glauber's salt) (Calculated from sodium determination)	6.17 gm.	in 100 c.c.
Saccharin		a trace.
Water (by difference) to make		100 c.c.

Secret nostrums—the so-called "patent medicines" sold to the public—are of two classes: One is harmless in itself, in that it contains but little or none of any medicinal substances and is potent for harm only in so far that it restrains the user from seeking competent treatment; the other not only keeps the sick person from receiving the treatment which is indicated, but contains ingredients which, when used indiscriminately, are potent for harm. Both classes are humbugs, especially because a large price is charged for what is usually worth but a few cents. In both classes there are all degrees of humbugs. "Liquid Life" easily belongs to the second class and is an example of the worst in this class. Besides containing the poisonous ingredient, zinc sulphate, its chief ingredient is Epsom salt, the long-continued use of which always does harm. When it is considered that during six years one patient consumed between $200 and $300 worth of the stuff (as sold at retail) the "degree" of the humbug may be appreciated.

In connection with the claim of the manufacturer that "Liquid Life" is "a true antitoxine" the following definitions for an antitoxin are given:

"A substance formed in the body, which neutralizes the poisonous products of a microorganism; a defensive proteid." (Standard Dictionary.)

"Any defensive proteid developed in the body as a result of the implantation of a poison, and acting as a neutralizer of the poison." (Dorland's Medical Dictionary.)

In view of these definitions and of the findings of the analysis, the absurdity of the claim that "Liquid Life" is "a true antitoxine" is patent.

Inasmuch as the courts have recently ruled that under the present Food and Drugs Act it is permissible to lie as to the curative properties of a preparation so long as no false statements concerning its composition are made, it would be interesting to know whether the assertion that the remedy contains "a true antitoxine" would be considered as a violation of the law; also whether the name "Liquid Life" would be held to be a false statement as to composition, or whether the learned justices would consider the name (although a deliberate lie) a permissible claim for the virtues of the remedy.

Details of Analysis

By appropriate tests, the presence of magnesium, sodium, as sulphate, saccharin, quinin and zinc was demonstrated. Cocain and morphin and their derivatives and substitutes were absent. Ammonia was absent.

Quinin.—Quinin was determined as follows: Two hundred c.c. of the material were acidified with hydrochloric acid, the solution filtered, the filter washed, the filtrate and washings united and diluted to 1,000 c.c. To portions of this solution, sufficient ammonia water and an excess of ammonium chlorid test solution were added, and the mixture shaken with successive portions of chloroform until extraction was completed. The chloroform solutions were washed with water, united and the mixture shaken with successive portions of 2 per cent. sulphuric acid until extraction was completed. The acid solutions were united, made alkaline with ammonia water, extracted with chloroform, the solvent evaporated, the residue dried at 100 C. and weighed. From 200 c.c. of the diluted solution, representing 40 c.c. original solution, 0.0157 gm. anhydrous quinin was obtained, equivalent to 0.055282 gm. crystallized quinin sulphate $[(C_{20}H_{24}O_2N_2)_2H_2SO_4 + 7H_2O]$ in each 100 c.c. of original solution. From 100 c.c. of the diluted solution, representing 20 c.c. of the original solution 0.0086 gm. anhydrous alkaloid was obtained, equivalent to 0.057865 gm. crystallized quinin sulphate in 100 c.c. of the original solution. Average, 0.056573 gm. quinin sulphate in 100 c.c. of the original solution.

Zinc Sulphate.—To an aliquot portion of the diluted solution, an excess of ammonium chlorid test solution and of ammonia water were added, and the solution saturated with hydrogen sulphid. The precipitate of zinc sulphid was dissolved in warm, diluted hydrochloric acid, the solution made alkaline with ammonia water and the zinc again precipitated by hydrogen sulphid. The precipitate was collected on a filter, washed with hydrogen sulphid test solution, dissolved in warm diluted hydrochloric acid, the resultant solution boiled until odorless and an excess of sodium carbonate test solution added. The precipitate was collected in a tared Gooch crucible, washed with hot water, dried, heated to low redness for fifteen minutes, cooled, weighed, and the weight of zinc oxid calculated to crystallized zinc sulphate. From 500 c.c. of the diluted solution, representing 100 c.c. of the original solution, 0.0683 gm. zinc oxid was obtained, equivalent to 0.241317 gm. crystallized zinc sulphate ($ZnSO_4+7H_2O$). From 200 c.c. of the diluted solution, representing 40 c.c. of the original solution, 0.0274 gm. zinc oxid was obtained, equivalent to 0.242024 gm. crystallized zinc sulphate in 100 c.c. of the original solution. Average 0.24167 gm. crystallized zinc sulphate in 100 c.c. of the original solution.

Magnesium Sulphate.—One of the solutions from which the zinc had been removed was acidified with hydrochloric acid, evaporated to small bulk, filtered and made up to 500 c.c. To aliquot portions of this solution ammonia water and sodium phosphate test solution were added in slight excess, the mixture allowed to stand twenty-four hours, the precipitate collected, washed and heated in the usual way, weighed, and the weight of the magnesium pyrophosphate calculated to crystallized magnesium sulphate ($MgSO_4—7H_2O$). From 10 c.c. of the diluted solution, representing 2 c.c. of the original solution, 0.1214 gm. magnesium pyrophosphate was obtained, equivalent to 0.26875 gm. crystallized magnesium sulphate, or 13.4375 gm. in 100 c.c. of the original solution. From a duplicate of 10 c.c. of the diluted solution 0.1197 gm. magnesium pyrophosphate was obtained, equivalent to 0.2650 gm. crystallized magnesium sulphate, or 13.25 gm. in each 100 c.c. Average, 13.34 gm. crystallized magnesium sulphate in each 100 c.c. of the original solution.

Sodium Sulphate. Sodium sulphate was determined by weighing as anhydrous sodium sulphate after elimination of the other metals by barium hydroxid and removal of the excess of barium by an excess of sulphuric acid. From 50 c.c. of a diluted solution of the material, representing 10 c.c. of the original solution, 0.3994 gm. anhydrous sodium sulphate was obtained, equivalent to 3.994 gm. in each 100 c.c. From 25 c.c. of a diluted solution of the material representing 2 c.c. of the original material, 0.0811 gm. anhydrous sodium sulphate was obtained, equivalent to 4.055 gm. in each 100 c.c. Average, 4.0245 gm. anhydrous sodium sulphate in each 100 c.c. of the original solution. This is equivalent to 6.17 gm. crystallized sodium sulphate in each 100 c.c. of the solution.

THE PREPARATION, QUALITY AND TESTING OF QUININ TANNATE

W. A. Puckner and L. E. Warren

Quinin is one of the very few specifics known to medicine. It is probably more used than any other single remedy. Because of the extremely bitter taste of its soluble salts its administration, especially to children, is a perplexing problem. Many

* Presented to the Section on Scientific Papers of the American Pharmaceutical Association, at the meeting held in Boston, Mass., Aug. 14-19, 1911.

attempts have been made to overcome this difficulty, but few of them are without objections. The administration of the alkaloid in capsules or coated tablets is fairly satisfactory, but most children and some adults cannot be induced to swallow these. Suspension of the alkaloid or some of its sparingly soluble compounds in flavored syrup has met with moderate success. Besides the alkaloid itself the most common combinations which are administered in this way are the sulphate, salicylate, tannate and certain esters.

Quinin tannate has been known in medicine for a very long time and the literature concerning it, although chiefly of pharmaceutical interest, is extensive. It is employed chiefly because it exhibits the quinin in an extremely insoluble form, one part of the salt requiring several thousand parts of cold water for solution. The salt is official in the Austrian, Danish, Dutch, German, Hungarian, Russian, Spanish and Swiss pharmacopeias. Numerous methods have been proposed for the preparation of quinin tannate. In most of them quinin sulphate is employed as the starting point. This is dissolved in very dilute sulphuric acid and the solution precipitated with a solution of tannic acid containing a small amount of alkali, usually sodium bicarbonate or ammonia. In other methods the acetate or the hydrochlorid of the alkaloid is employed and in some the precipitation is made in a hydroalcoholic menstruum. The precipitate is then freed from soluble impurities more or less completely by washing.

Since the literature of quinin tannate is so voluminous, and since it deals for the most part with unimportant modifications of processes for making the salt, no attempt is here made to review any except a few of the more important papers.

Between the years 1875 and 1885 Rozsnay,[1] a Hungarian pharmacist, perfected a process for preparing quinin tannate which produces a salt of great purity. For a time the method remained a secret, but later the details became known and the process has now been incorporated in several of the pharmacopeias. By the process which Rozsnay introduced the salt is prepared by precipitation in the usual way, is washed with a small quantity of water and is then melted in hot water. By this process the small individual particles coalesce and the substance is thereby rendered less bitter. On pouring off the supernatant liquid the quinin tannate is left as a resin-like mass which soon solidifies and may then be powdered and dried.

1. Pharm. Zentralhalle, 1875, xvi, 106; New Remedies, 1883, xii, 274

A process for preparing quinin tannate which was quite popular a quarter of a century ago deserves mention.[2] Quinin was first prepared by precipitation from the solution of the sulphate of the alkaloid with solution of sodium carbonate. The precipitate was washed and dissolved in alcohol. The alcoholic solution was then poured slowly into an aqueous solution of tannic acid. The precipitate after washing and drying was light in color and practically tasteless. Because of its expensiveness, owing to the alcohol used, and because of the low alkaloidal content of the finished product (about 20 per cent.), the method is no longer used.

The therapeutic efficiency of quinin tannate has been questioned. Many years ago Hager[3] reported that from the results of experiments on his own person and on others, he had concluded that this salt has only about one-tenth of the value of quinin sulphate. His conclusions, however, cannot be considered authoritative, since he states that nine-tenths of the alkaloid may be recovered from the urine and feces. He evidently assumes that the alkaloid eliminated by the urine is inert, a conclusion which in the light of present knowledge is not justified.

Some years after Hager's report was published, Field[4] experimented with the solubility of quinin tannate in gastric juice. He prepared artificial gastric juice and also collected the natural secretion from a healthy dog. He attempted to dissolve the quinin tannate in these solutions, but found that the salt was practically insoluble. From the results of his experiments, which also included the administration of the drug to the human subject, the author concluded that quinin tannate is practically inert as a medicinal substance. It would appear that this conclusion, so far as it is based on the solubility of the salt in gastric juice, is untenable because the salt is prepared by precipitation from a slightly acid solution, and it could not, therefore, be expected to dissolve appreciably in gastric juice. Field pointed out that even if the salt were absorbed in the stomach of the patient, the ingestion of such large proportions of tannic acid might be very undesirable.

On the other hand, Zeig[5] contends that the salt is active. He states that if a grain of the salt be dissolved in an ounce of very dilute hydrochloric acid at a temperature of 140 F.

2. Pharm. Zentralhalle, 1882, xxiii, 250; Am. Druggist, 1887, xvi, 68.

3. Pharm. Zentralhalle, 1872, xiii, 247; Proc. Am. Pharm. Assn., 1873, xxi, 379.

4. Phys. Surg., 1883, v, 353; Pharm. Rec., 1884, iv, 5; Proc. Am. Pharm. Assn., 1884, xxxii, 308.

5. West. Druggist, 1893, xv, 361; from Proc. Cal. Pharm. Assn., 1892; Proc. Am. Pharm. Assn., 1894, xlii, 651.

(60 C), the solution will possess a taste as bitter as that of a control using an equivalent amount of quinin sulphate.

Christian[6] working in Koch's clinic has studied the efficiency of some of the difficultly soluble quinin salts and esters. He administered known quantities of the alkaloidal combination, collected the urine of the patients and extracted the alkaloid therefrom, the percentage of alkaloid excreted being considered as the efficiency criterion. While a number of experiments were carried out with such compounds as euquinin and saloquinin only two tests with quinin tannate were recorded. From one of these 13.18 per cent. of the alkaloid given was recovered and from the other 23.79 per cent.

From the conflicting results of these inadequate and for the most part unscientific experiments, it can be seen that the question of the therapeutic efficiency of the salt is still an open one. It is to be hoped that the value of quinin tannate will be determined by scientific experimentation.

But few reports of examinations of commercial quinin tannate have appeared. In 1878 Jobst[7] examined several specimens of the preparation, the method of manufacture of which was unknown to him, and at the same time several factory specimens of known origin were studied. The examination revealed great variations in composition, not only in respect to the content of water and total alkaloid, but also in the kind of alkaloid, as several of the commercial specimens contained mixtures of the cinchona alkaloids. His findings are tabulated below:

Method of Manufacture.	Water (loss at 120 C.), per cent.	Quinin, per cent.	Quinidin, per cent.	Cinchonidin, per cent.	Cinchonin, per cent.
Known	7.2	31.37	....	....	....
Known	9.7	22.72	....	....	....
Known	10.7	10.00	....	....	....
Known	11.4	7.40	....	....	....
Unknown	9.1	4.46	11.97	7.33	....
Unknown	9.8	4.93	2.43	13.10	3.35
Unknown	10.2	6.23	trace	20.80	trace

He assigns the formula, $C_{20}H_{24}O_2N_2.2C_{14}H_{10}O_4 + 4H_2O$, as the most probable one for the salt having the highest quinin con-

6. Deutsch. Wchnschr., 1903, xxix, 216.
7. Arch. Pharm., 1878, ccxii, 331; Proc. Am. Pharm. Assn., 1878, xxvi, 578.

tent, viz., 31.37 per cent. The total alkaloidal content was determined by mixing with freshly slaked lime, drying and extracting the pulverized mass with chloroform. As the author's methods for the quantitative separation of the several alkaloids are not given, no estimate of the accuracy of the recorded results can be made. Water was determined by drying at 120° C. From the results of his experiments, he concluded that tannic acid is capable of forming very variable compounds with quinin according to the proportion and manner in which it is employed in the manufacture of the combination. To obtain products of even an approximately constant composition, definite quantities of tannic acid and of quinin must always be employed.

In 1889 Neumann[8] examined four commercial specimens of quinin tannate while testing a method which he had worked out for the assay of the product. The quinin content varied between 13.9 per cent. and 28.8 per cent., three of the specimens assaying more than 25 per cent. of the alkaloid. These results, however, could not be considered as authoritative, as controls indicated that the method gave values about 3 per cent. too high.

In 1892 Zeig[9] stated that he had found the alkaloidal content of commercial specimens of quinin tannate to vary between 10 and 25 per cent., but he gave no information concerning the number of specimens examined nor of the names of the brands studied.

Quinin tannate having been considered by the Council on Pharmacy and Chemistry of the American Medical Association, the Association laboratory took up the examination of the several brands of the product on the American market. At the same time specimens of the salt were prepared by various methods, and these were included in the examination. Tentative academic standards for the substance were prepared and submitted for criticism to several manufacturers of pharmaceutical chemicals whom it was thought might be interested.

LABORATORY SPECIMENS

The method of manufacture first employed was that of the Swiss Pharmacopeia. Briefly, the method is as follows:

Nine parts of quinin sulphate are dissolved in a mixture consisting of 16 parts of diluted sulphuric acid and 300 parts of

8. Zeit. anal. Chemie, 1889, xxviii, 663; Proc. Am. Pharm. Assn., 1890, xxxviii, 673.

9. West. Druggist, 1893, xv, 361; from Proc. Ca. Pharm. Assn., 1892; Proc. Am. Pharm. Assn., 1894, xlii, 651.

water. Twenty one parts of tannic acid and 3.5 parts of sodium bicarbonate are dissolved in 300 parts of water without the application of heat. This solution is poured with constant stirring into the solution of quinin sulphate. The resultant precipitate is washed with water until the washings, after acidification with nitric acid, cease to give a turbidity with barium nitrate solution.

In preparing the salt by this method it was found impracticable to follow the directions concerning the washing to completion, as the precipitate was of such bulk that the sulphate could not be completely removed. Although the standard of the Swiss Pharmacopeia requires that the salt shall contain from 30 to 35 per cent. of quinin, the laboratory specimen prepared as above contained but about 25.8 per cent. of alkaloid. Quinin was determined by suspending the salt in weak ammonia water, shaking the mixture with successive portions of chloroform until extraction was complete, evaporating the solvent, drying the residue at 100 C. and weighing the alkaloid.[10] Water was determined by drying at 100 C. This specimen lost 7.6 per cent. of its weight on drying. In the appended table of analytical results it is designated as "No. 1."

The New York Quinin and Chemical Works, a leading manufacturer of quinin salts, having criticized the Swiss method of manufacture (the method included in the tentative academic standards which were submitted to the manufacturers), in respect to the proportions of the several ingredients used, a specimen was prepared in the laboratory by the Swiss method, but using the quantities suggested by this manufacturer, which were as follows:

Quinin sulphate	8.4 parts
Diluted sulphuric acid	15.0 parts
Tannic acid	15.0 parts
Sodium bicarbonate	3.0 parts

The manufacturer stated that these proportions would yield a product corresponding very nearly to the formula, $C_{20}H_{24}O_2N_2(HC_{14}H_9O_9)_2 + 4H_2O$, and containing 31.16 per cent. of anhydrous quinin, 61.91 per cent. of tannic acid and 6.93 per cent. of water. The laboratory specimen prepared according to the manufacturer's suggestion contained 31.3 per cent. of alkaloid and lost 9.0 per cent. of its weight on drying. This specimen is designated as "No. 2" in the table of analytical results.

Quinin tannate was prepared by the method of the Hungarian Pharmacopeia, aliquot parts of the prescribed quantities being used. The following is the method as used:

10. This method is described in greater detail in the tentative description for Quinin Tannate given elsewhere in this paper.

Ten parts of quinin sulphate are dissolved in 150 parts of distilled water by the aid of the smallest necessary quantity of diluted sulphuric acid. Twenty parts of tannic acid are dissolved in 140 parts of water and the filtered solution poured with constant stirring into the solution of quinin sulphate. A mixture of 5 parts of tannic acid, 80 parts of water and 5 parts of ammonia water is filtered and poured slowly and with constant stirring into the quinin-tannin mixture prepared as above described. The resultant precipitate is collected on a filter and washed with 80 parts of water. The mass is then gently expressed and warmed with 40 parts of water until it melts to a resin-like mass. It is then dried and pulverized.

Although the Hungarian Pharmacopeia requires that the salt shall contain from 30 to 32 per cent. of anhydrous quinin the laboratory specimen prepared as above described contained but about 25 per cent. of alkaloid. The loss on drying amounted to about 10.0 per cent. of the weight of substance taken. In the table of analytical results this specimen is designated as "No. 3."

The salt was then prepared by the method of the Hungarian Pharmacopeia except that the quantities of the several ingredients used were modified to conform to the proportions employed in the preparation of "No. 2." Ammonia water was used as the precipitant. The following quantities were used:

Solution 1:		
Quinin sulphate	5.4	gm.
Diluted sulphuric acid	15.5	c.c.
Water	150	c.c.
Solution 2:		
Tannic acid	10	gm.
Water	70	c.c.
Solution 3:		
Tannic acid	3	gm.
Ammonia water	5	c.c.
Water	50	c.c.

This laboratory specimen prepared as above contained 28.7 per cent. of alkaloid and lost 10.0 per cent. of its weight on drying. The specimen is designated as "No. 4" in the table of analytical results.

Another specimen was prepared exactly like "No. 4" except that sodium bicarbonate was used as the precipitant instead of ammonia water, 3 gm. being used. This specimen contained 33.3 per cent. of alkaloid and lost 7.2 per cent. of its weight on drying. It is designated as "No. 5" in the table of analytical results.

Quinin tannate was prepared by the method official in the German Pharmacopeia. Essentially this is the Rozsnay method, official in the Hungarian Pharmacopeia, but it has been mod-

ified in one important particular. It is directed that after the salt has been dried in a warm place, it is to be dried at 100 C. The preparation of a specimen by this method was begun and completed through the stage of drying at 30 C. to 40 C. The air-dried specimen was then divided into two equal portions and one of them was dried at 100 C. as directed. The two subdivisions were then compared. The air-dried specimen was a drab colored, moderately bulky powder which did not adhere to the surfaces of glass or paper. It contained 25.8 per cent. of quinin and the loss on drying at 100 C. amounted to 9.8 per cent. The portion which had been dried at 100 C. was somewhat darker in color than the other, was slightly less bulky, and adhered to glass and paper in a very troublesome way. It contained 27.8 per cent. of quinin. These specimens are respectively designated in the table of analytical results as "No. 6" and "No. 6-a." The German Pharmacopeia requires that the salt shall contain at least 30 per cent. of quinin.

Another specimen was prepared by the following method:

Ten gm. of quinin sulphate are dissolved in a mixture of 15 c.c. of diluted sulphuric acid and 300 c.c. of water. Twelve gm. of tannic acid are dissolved in 100 c.c. of water and the filtered solution poured slowly and with constant stirring into the solution of quinin sulphate. Six gm. of tannic acid are then dissolved in 50 c.c. of water and 2 gm. of sodium bicarbonate dissolved in the solution. This solution is filtered and the filtrate poured slowly and with constant stirring into the quinin-tannate mixture, prepared as above described. The precipitated quinin tannate is allowed to stand for twenty-four hours. It is then poured on a muslin filter, washed with 100 c.c of water and expressed with moderate pressure. The expressed mass is then transferred to a porcelain dish, 100 c.c. of water added and the mixture heated on the water bath until the quinin tannate melts to a resin-like mass. The supernatant liquid is poured off, the mass dried in the air and pulverized.

This specimen contained 29.3 per cent. of alkaloid and lost 7.9 per cent. of its weight on drying. It is designated as "No. 7" in the tabulated analytical results.

As it seemed probable that the amount of sodium bicarbonate was too small to obtain a salt containing the maximum amount of alkaloid, the experiment was repeated with some variations. Three gm. sodium bicarbonate were employed instead of two and the amounts of solvent in some cases were changed. The details of the variations may be seen by consulting Table 1. This process yielded 22.2 gm. ofthe salt (from 10 gm. of quinin sulphate), and the specimen ("No. 8" in Table II) contained 29.1 per cent. of alkaloid and the loss on drying amounted to 7.3 per cent.

In the hope of obtaining a salt with a higher alkaloidal content another specimen was prepared by the same method as was used in "No. 8" except that 4 gm. of sodium bicarbonate were used as the precipitant. The quantities of the several ingredients used may be seen by consulting Table I. This specimen was very dark colored and otherwise objectionable in appearance. The yield was less than that obtained by some of the other methods and the product was less bulky. It contained 34.2 per cent. of quinin and lost 8.1 per cent. of its weight on drying. This specimen is designated as "No. 9" in Table II.

Another specimen was prepared by a method which is very similar to that used in the preparation of "No. 8," the quantities of the several ingredients used being given in Table I. This specimen contained 33.7 per cent. of alkaloid and lost 7.7 per cent. of its weight on drying. It is designated as "No. 10" in Table II.

A general idea of the variations in the processes used in the preparation of the several specimens may be gained by a study of Table I. In this table the composition is given of the several "solutions" used in the manufacture of each specimen. It is to be understood of course that precipitation is brought about by mixing the several solutions.

From the results of the experimental work it is concluded that it is easily possible to obtain quinin tannate containing over 30 per cent. of anhydrous quinin but that this desideratum is not attainable if the substance be prepared by any of the methods now official in the pharmacopeias. Sodium bicarbonate is more satisfactory as a precipitant than ammonia water but it is essential that an excess of the alkali be avoided. While the observations and experiments are too few to warrant a positive conclusion it appears that if ammonia water be used as the precipitant the yield of the finished product will be larger than is the case when sodium bicarbonate is employed. The quinin content, however, is proportionately smaller. The observation of Jobst that in order to obtain products of even an approximately constant composition it is necessary to employ definite proportions of tannic acid and of quinin has been confirmed by our experiments.

COMMERCIAL SPECIMENS

Four specimens of quinin tannate bearing the labels of as many manufacturers were purchased and examined with particular reference to the alkaloidal content and to the loss on

TABLE I

Solution		1	2	3	4	5	6	7	8	9	10
1	Quinin sulphate	9	8.4	10 gm.	8.4 gm.	8.4 gm.	4 gm.	10 gm.	10 gm.	10 gm.	10 gm.
	Dil. sulphuric acid	16	15.0	q. s.	15.5 c.c.	15 c.c.	q. s.	15 c.c.	15 c.c.	15 c.c.	15 c.c.
	Water	300	300	150	150 c.c.	150 c.c.	120 c.c.	300 c.c.	150 c.c.	150 c.c.	150 c.c.
2	Tannic acid			20 gm.	10 gm.	10 gm.	8 gm.	12 gm.	12 gm.	12 gm.	12 gm.
	Water			140 c.c.	70 c.c.	70 c.c.	50 c.c.	100 c.c.	100 c.c.	75 c.c.	75 c.c.
3	Tannic acid	21	15			3 gm.		6 gm.			
	Sodium bicarb.	3.5	3			3 gm.		2 gm.			
	Water	300	300			50 c.c.		50 c.c.			
4	Tannic acid			5 gm.	3 gm.		2 gm.				
	Ammonia water			5 c.c.	5 c.c.		2 c.c.				
	Water			80 c.c.	50 c.c.		32 c.c.				
5	Sodium bicarb.								8 gm.	4 gm.	8 gm.
	Water								40 c.c.	50 c.c.	50 c.c.
6	Tannic acid								8 gm.	8 gm.	8 gm.
	Water								25 c.c.	50 c.c.	50 c.c.

drying at 100 C. The specimen bearing the label of the Powers-Weightman-Rosengarten Co. contained 29.3 per cent. of anhydrous quinin, and the loss on drying the specimen amounted to 7.9 per cent. of the original weight. The specimen put up under the label of the Brunswick Chemical Works, but bearing the label of the Mallinckrodt Chemical Works as selling agent, contained 29.5 per cent. of quinin and the loss on drying amounted to 6.5 per cent. The specimen bearing the New York Quinin and Chemical Works label contained about 33.4 per cent. of alkaloid and the loss on drying amounted to 8.0 per cent. The Merck brand contained about 34.0 per cent. of total alkaloid and the loss on drying amounted to 9.0 per cent. This specimen contained a considerable quantity of uncombined alkaloid, reference to which will again be made.

The amount soluble in anhydrous ether under specified conditions was determined, not only in the specimens purchased but also in those prepared in the laboratory. Tests for chlorid and sulphate were also carried out and an attempt was made to obtain some idea of the relative bitterness of the several specimens examined.

Ether-Soluble: Preliminary tests indicated that one of the specimens contained considerable amounts of uncombined alkaloid. Accordingly the amount soluble in dry ether was determined as follows:

Two gm. of quinin tannate were [illegible] anhydrous ether poured upon it and the mixture stirred with a glass rod. After allowing the suspended salt to settle the supernatant liquid was poured through a dry filter into a tared flask. The insoluble residue was similarly treated twice more with 25 c.c. portions of dry ether and the filter finally washed with 10 c.c. of the solvent. The united filtrates were distilled, the residue dried at 100 C. and weighed. As quinin tannate is slightly soluble in anhydrous ether, a weighable residue may always be expected.

When tested by the above-described method the several specimens with a single exception gave residues varying not far from 0.1 per cent. to 0.3 per cent. One specimen (Merck brand) contained about 9 per cent. of ether-soluble matter, which latter appeared for the most part to consist of free alkaloid.

Chlorid and Sulphate: One gm. of quinin tannate was thoroughly shaken with 100 c.c. of water and the mixture allowed to settle. The supernatant liquid was poured through a filter, the filtrate acidified with diluted nitric acid and the usual tests for chlorid and sulphate applied. With one exception each specimen contained appreciable amounts of sulphate and traces of chlorid. In this one exception sulphate was absent but con-

siderable amounts of chlorid were present, thus indicating the probable source from which the salt had been prepared.

Bitterness: One gm. of the salt was shaken with 100 c.c. of water and filtered. The filtrates from several specimens were then compared by tasting. While none of the filtrates were free from bitterness in general the relative bitterness was found to coincide with the relative turbidity found in the tests for chlorid or sulphate. The Merck specimen which contained a large amount of free alkaloid, was much more bitter than any of the others although it is described on the label as "Neutral-Tasteless."

The results found from the several specimens examined are tabulated on page 57.

From the results of the examination it is seen that commercial quinin tannate varies somewhat in composition. Doubtless this is due to slight differences in the manufacturing methods of the various makers. However, with the exception of the Merck specimen, which bears evidence of careless manufacture, the several makes of quinin tannate on the American market may, on the whole, be regarded as of sufficiently uniform composition for practical purposes.

Based on the provisional academic standards as first prepared but modified as found necessary by the results of the experimental work, and by the suggestions offered by those to whom the provisional description was submitted for criticism, tentative standards for quinin tannate have been prepared. Our thanks are due to those manufacturers who have made suggestions and criticisms in the preparation of these provisional standards for quinin tannate. The description and standards suggested are as follows:

QUININ TANNATE—Quininæ Tannas. Quinin tannate is the tannate of the alkaloid, quinin, containing from 30 to 35 per cent. of quinin.

Quinin tannate may be prepared as follows:

Ten gm. of quinin sulphate are dissolved in a mixture of 15 c.c. of diluted sulphuric acid and 150 c.c. of water. Twelve gm. of tannic acid are dissolved in 75 c.c. of water and the filtered solution poured slowly and with constant stirring into the solution of quinin sulphate. Three gm. of tannic acid are then dissolved in 50 c.c. of water and 3 gm. of sodium bicarbonate dissolved in 50 c.c. of water. These solutions are filtered, the filtrates mixed, and the mixture poured slowly with constant stirring into the quinin-tannin mixture prepared as above described. The precipitated quinin tannate is allowed to stand for twenty-four hours. It is then poured onto a muslin filter, washed with 100 c.c. of water and expressed with moderate pressure. The expressed mass is then transferred to a porcelain dish, 50 c.c. of water added and the mixture heated on the water bath until the quinin tannate melts to a resin-like mass.

TABLE II.

Number or Brand.	Anhydrous Quinin.	Water (Loss at 100 C.)	Ether Soluble.	Sulphate.	Chlorid.	Taste of Filtrate.	Yield (in gm.) Calculated from 10 gm. Quinin Sulphate.	Remarks.
1	25.75	7.64	0.17	Very marked turbidity.	Noticeable opalescence.	Noticeably bitter..	....	
2	31.33	9.01	0.08	Very marked turbidity.	Very faint opalescence.	Noticeably bitter..	....	
3	25.02	9.96	0.10	Faint turbidity...	Very faint opalescence.	Slightly bitter....	....	
4	28.70	9.96	0.05	Marked turbidity.	Very faint opalescence.	Slightly bitter....	31.0	
5	33.31	7.20	0.11	Faint turbidity...	Very faint opalescence.	Slightly bitter....	....	
6	25.85	9.78	0.08	Faint turbidity...	Very faint opalescence.	Slightly bitter....	28.8	
6a	27.82	....	0.09	Faint turbidity..	Very faint opalescence.	Slightly bitter....	26.0	Adheres to glass and paper.
7	29.33	7.94	0.09	Faint turbidity...	Very faint opalescence.	Slightly bitter....	....	
8	29.12	7.35	0.12	Faint turbidity...	Very faint opalescence.	Slightly bitter....	23.2	Dark color.
9	34.25	8.12	0.09	Faint turbidity...	Very faint opalescence.	Slightly bitter....	20.0	
10	33.72	7.74	0.08	Faint turbidity...	Very faint opalescence.	Slightly bitter....	20.6	
P. W. R. ..	29.30	7.88	0.10	Distinct turbidity.	Noticeable opalescence.	Noticeably bitter..		
Brunswick (M. C. W.)	29.51	6.50	0.19	Absent	Very marked opalescence.	Noticeably bitter..	....	Evidently prepared from quinin hydrochlorid.
N. Y. Q. ...	33.36	8.05	0.36	Distinct turbidity.	Noticeable opalescence.	Noticeably bitter..	....	
Merck	33.97	9.06	9.02	Very faint opalescence.	Very faint opalescence	Very bitter.....		

The supernatant liquid is poured off, the mass cooled, dried in air and pulverized.

Quinin tannate is an amorphous, pale lemon-yellow to yellowish-white, odorless powder without taste, or at most slightly bitter, and with scarcely any astringency. It is slightly soluble in water, ether and chloroform, but somewhat more soluble in alcohol. The aqueous and alcoholic solutions are colored bluish-black by ferric chlorid test solution. Quinin tannate melts on heating in a glass tube to a purplish, tar-like material.

If 1 gm. of quinin tannate be shaken with a mixture of 50 c.c. of water and 1 c.c. of nitric acid and the mixture filtered, a portion of the filtrate should not become more than slightly opalescent after the addition of 1 c.c. of silver nitrate test solution; nor should there by any darkening after the addition of 1 c.c. of hydrogen sulphid test solution; nor should a portion be rendered turbid immediately by barium chlorid test solution.

If from 0.5 gm. to 1 gm. of quinin tannate be mixed with 25 c.c. of water and an excess of ammonia water, the mixture extracted with three successive portions of 20 c.c. each of chloroform, the total solvent washed with water and evaporated, the weight of residue obtained after drying at 100 C. should correspond to from 30 to 35 per cent. of anhydrous quinin. If this residue be dissolved in 30 c.c. of water by the aid of a few drops of diluted hydrochloric acid and 1 c.c. of the solution be mixed with 20 c.c. of water and 2 or 3 drops of bromin test solution, the mixture should assume a green coloration on the addition of ammonia water.

If 0.2 gm. of quinin tannate be ignited no weighable residue should be obtained.

If from 0.5 gm. to 1 gm. of quinin tannate be dried at 100 C. to constant weight the loss should not correspond to more than 10 per cent. of the weight of substance taken (absence of an undue amount of *water*).

If 2 gm. of quinin tannate be shaken with three successive portions of 25 c.c. each of anhydrous ether, the solvent poured through a filter, the filter washed with 10 c.c. of the solvent, the several filtrates united, evaporated and the residue dried to constant weight at 100 C. the weight of the residue should not exceed 0.005 gm. (limit of *uncombined alkaloid*).

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1878—Jobst: Arch. Pharm., ccxii, 331; Proc. Am. Pharm. Assn., xxvi, 578 (1878). Report of an examination of several specimens of commercial quinin tannate.

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1878—Berwick: Am. Jour. Pharm., l, 259; from Pharm. Ztg. (1878). Proc. Am. Pharm. Assn., xxvi, 578 (1878). Process for manufacturing quinin tannate.

1882—Dukla: Pharm. Jour. Tr., [3], xiii, 444; from Pharm. Ztg. (1882). Process for manufacture of the salt by the alcohol solvent method.

1882—Anonymous: New Remedies, xi, 173; Proc. Am. Pharm. Assn., xxx, 414 (1882). Review of a process of manufacture which employs acetate of ammonia. Product contains 19 to 21 per cent. of quinin.

1882—Fiebert: Pharm. Zentralhalle, xxiii, 550; from Zeit. öest. Ap. Ver. (1882). Proc. Am. Pharm. Assn., xxxi, 273 (1882). Process of manufacture by the alcohol solvent method.

1883—Rosznay: Proc. Am. Pharm. Assn., xxxii, 308; from Gy. Rund. (1883). New Rem., xii, 274 (1883). A method of assay. Substance is mixed with calcium and sodium hydroxids, dried and the mass extracted with chloroform.

1883—Rother: Am. Jour. Pharm., lv, 172. Maintains that the compounds of quinin and tannic acid are not true salts, but are analagous to the alcoholates. Suggests that they be called "tannolates." Theoretical composition discussed.

1883—Weiss: Proc. Am. Pharm. Assn., xxxii, 84 (1884); from Pharm. Ztg. (1883). Describes a method for preparing a finely divided quinin tannate in a syrup.

1883—Field: Phys. Surg., v, 353; Pharm. Rec., iv, 5 (1884). Proc. Am. Pharm. Assn., xxxii, 308 (1884). Experiments with the solubility of quinin tannate in gastric juice.

1885—Schwarz: Pharm. Zentralhalle, xxvi, 471; from Pharm. Ztg. (1885). Proc. Am. Pharm. Assn., xxxiv, 605 (1886). Apparently the first to employ sodium bicarbonate as a precipitant in the manufacture of quinin tannate. Produced a specimen containing 33.3 per cent. of quinin.

1885—Peltz: Pharm. Ztschr. Russ., xxiv, 80; Proc. Am. Pharm. Assn., xxxiii, 303 (1885). Recommends the use of quinin hydrochlorid in place of the sulphate in the manufacture of quinin tannate.

1889—Neumann: Zeit. anal. Chemie, xxviii, 663; Proc. Am. Pharm. Assn., xxxviii, 673 (1890). Describes a process for the

alkaloidal assay of quinin tannate. Controls indicate that the method gives values about 3 per cent. too high. Examined several commercial specimens, the alkaloidal content of which (as found) ranged from 13.9 per cent. to 28.8 per cent.

1891—De Vrij: Ned. Tidjdschr., iii, 113; Proc. Am. Pharm. Assn., xl, 744 (1892). A method of preparation is described.

1892—Zeig: West. Druggist, xv, 361 (1893); from Proc. Cal. Pharm. Assn. (1892). Proc. Am. Pharm. Assn., xlii, 651 (1894). States that commercial quinin tannate contains from 10 per cent. to 25 per cent. alkaloid. Believes that the salt is sufficiently soluble in gastric juice to be therapeutically active.

1893—Drake: Proc. Am. Pharm. Assn., xlii, 675 (1894); from Proc. Mass. Pharm. Assn. (1893). Describes a process of manufacture in which no alkali is employed.

1894—De Vrij: Pharm. Zentralhalle, xxxv, 155; Proc. Am. Pharm. Assn., xlii, 1108 (1894). Describes a process for preparing the salt.

1898—Rosenheim and Schidrowitz: Jour. Chem. Soc., lxxiii, 878. Find that the specific rotatory power of quinin tannate in methyl alcohol solution at 15 C. is — 40.1°.

1898—Schidrowitz: See Rosenheim.

1900—Zeelt: Pharm. Ztg., xlv, 96; from Pharm. Wkblad. (1900). Proc. Am. Pharm. Assn., xlviii, 813 (1900). Describes a process for manufacturing quinin tannate.

1903—Christian: Deutsch. med. Wchnschr., xxix, 216. Administered known quantities of quinin tannate to human beings and recovered the alkaloid excreted in the urine. In each of two experiments he recovered less than 25 per cent. of the total alkaloid given.

1906—Fränkel: Die Arzneimittel-Synthese, ed. 2, 140 (1906). Calls attention to the possible undesirability of the large proportion of tannin in quinin tannate.

1906—Nierenstein: Chem. Central-Blatt, lxxvii, I, 1417 (1906); from Collegium (1906). Amorphous quinin tannate melts at 62-64 C.; it may be crystallized from ether by the addition of acetic anhydrid; crystallized substance melts at 79-81 C.

1909—Biginelli: Pharm. Ztg., liv, 726 (1909); from Gaz. chim. ital. (1909). There are four quinin tannates, viz.: tetraquinin pentannate, biquinin tritannate, biquinin tetratannate and biquinin pentannate.

1909—Calliers: Ap. Ztg., xxiv, 159; Pharm. Zentralhalle, l, 263, 607 (1909). Describes a method of assay.

1910—Cohn: Pharm. Zentralhalle, li, 265; Year-Book Pharm., 12 (1910). Method for manufacture.

1911—May: Chem. Syn. Drugs, 84 (1911). Mentions that quinin tannate is but slowly split up in the intestine and for this reason it is lacking in therapeutic prompitude and certainty.

CALCIUM PHENOLSULPHONATE

W. A. Puckner and L. E. Warren

(*Reprinted, with additions, from The Journal A. M. A., Oct. 21, 1911, p. 1383*)

The examination of calcium phenolsulphonate (calcium sulphocarbolate) was taken up at the request of the Council. Tentative standards for the substance were prepared and after the examination of the specimens had been completed, these standards were submitted for criticism to several manufacturers of chemicals. At the same time the findings (for each manufacturer's product) which were not in accord with

the proposed standards were submitted to the manufacturers interested.

The product was examined with reference to the residue on ignition, loss on drying at 100 C., freedom from arsenic and heavy metals, sulphates and uncombined phenol. Some of the specimens studied were purchased on the open market while others were furnished by the manufacturers. The tests for purity to which the product was subjected are as follows:

TESTS

An aqueous solution of the salt (1-100) should not respond to the time-limit test for *heavy metals* prescribed by the United States Pharmacopeia, 8th Revision.

An aqueous solution of the salt (1-100) acidified with a few drops of diluted hydrochloric acid should give no immediate turbidity after the addition of 1 c.c. of barium chlorid test solution (limit of *sulphate*).

If 5 gm. of the salt be percolated with 25 c.c. of ether in a small filter, the solvent allowed to evaporate spontaneously and the residue, if any, dissolved in 5 c.c. of water, the solution should not give a white precipitate on the addition of a few drops of bromin test solution (absence of *phenol*).

If dried at 100 C. (212 F.) for 1 hour the salt should not lose more than 2 per cent. of its weight (absence of an undue amount of *water*).

If from 0.5 to 1 gm. of the salt be dried to constant weight at 100 C. (212 F.) and the dried substance be slowly ignited in an uncovered crucible (care being taken that the contents be freely exposed to the air) until the weight becomes constant, the residue should amount to not less than 35.0 per cent., nor more than 36.0 per cent. of the weight of the dried substance.

The results of the examination are tabulated on page 62.

These results show that commercial calcium phenolsulphonate varies somewhat in purity and uniformity of composition. The formula commonly assigned to the salt in most text books of pharmaceutical chemistry is $Ca(C_6H_5O_4S)_2 + H_2O$. Theoretically such a salt should contain 4.45 per cent. of water and should yield 33.68 per cent. of residue on ignition. The above formula is given in Merck's Index (1907), yet the market product bearing the label of this firm was found to contain only 0.45 per cent. water and was therefore, not the monohydrated salt indicated by the formula.

The results of our examination were then transmitted to the firms whose products had been examined.

Brand.	Water (Loss at 100° C.).	Residue on Ignition (Calculated from Dried Specimen).	Color.	Odor.	Phenol Test.
M. C. W.[2]	0.42	35.18	Noticeably pinkish	Somewhat phenol like	Distinct precipitation.
M. & Co.[3]	0.45	35.28	Very faintly pinkish	Distinctly phenol like	Distinct precipitation.
A. A. Co.[4]	15.13	35.24	Faintly yellowish	Distinctly acetone like	None.
P. W. R.[5]	0.41	35.42	Faintly pinkish	Odorless	Distinct precipitation.

2. M. C. W.—Mallinckrodt Chemical Works.
3. M. & Co.—Merck & Company.
4. A. A. Co.—Abbott Alkaloidal Company.
5. P. W. R.—Powers Weightman Rosengarten Company.

The Mallinckrodt Chemical Works, in replying, wrote that its manufacturing department was experimenting in an attempt to produce a phenol-free salt at moderate cost. Some time later a specimen of this firm's latest product was sent to the laboratory for examination. This specimen lost 0.44 per cent. of its weight on drying and the dried material yielded 35.24 per cent. of residue on ignition, results that were well within the limits suggested in the standards proposed. The specimen did not respond to the bromin-water test for phenols and both in color and odor was superior to the first specimen of this firm's that was examined.

The Abbott Alkaloidal Co., in submitting its brand of calcium phenolsulphonate, gave the same formula to indicate the composition of its product as is found in Merck's Index, namely, $Ca(C_6H_5O_4S)_2+H_2O$. When the specimen was dried at 100 C., however, it lost about 15 per cent. of its weight, showing that it had a much larger water-content than was claimed by the manufacturer. This result was verified also by the amount of residue found on ignition, which amounted to 30 per cent. of the weight of the undried specimen instead of 33.68 per cent. as is required by the formula of the salt containing 1 molecule of water. These laboratory findings were sent to the firm. No acknowledgment was received for nearly six months and then the company wrote questioning the chemists' results and asserting that its product contained "about 4.5 per cent." (theoretically 4.45 per cent.) of water instead of the 15.1 per cent. as had been reported by us. This, of course, was a reiteration of the claim made at the time the product was submitted to the Council. In its letter, the company stated that it was sending another sample of calcium phenolsulphonate for further experimentation. This specimen lost 1.93 per cent. of its weight on drying and the dried material gave 35.15 per cent. of ash on ignition; it did not respond to the bromin-water test for phenol. These later results indicated that, although the firm was ignorant of the composition of its own product, the second specimen complied with the proposed standard.

As the table shows, the products of Merck and Powers-Weightman-Rosengarten were both found to contain free phenol. These firms were advised of the laboratory's findings, but, beyond acknowledging the letters that were sent, they have taken no further action.

The results of the examination of calcium phenol-sulphonate illustrate what other examinations in the Association labora

tory have so often shown, viz., that commercial products which are but little used and for which there are no authoritative standards for strength and purity, are also invariably unreliable in composition.

Details of Analysis

Qualitative tests on all of the specimens indicated the presence of calcium and of combined phenolsulphonic acid. The usual tests for sulphate and for heavy metals gave negative results. Tests for uncombined phenol gave positive results on some of the specimens.

WATER:—Portions of the material were dried at 100 C. and the loss considered as water.

RESULTS.—*Mallinckrodt brand:* From 1.0027 gm. a loss of 0.0043 gm. was noted, equivalent to 0.43 per cent.; 1.0016 gm. lost 0.0042 gm. equivalent to 0.42 per cent.; average, 0.42 per cent. loss on drying. *Merck brand:* On drying 1.0004 gm. lost 0.0047 gm., equivalent to 0.47 per cent.; 1.0014 gm. lost 0.0044 gm. equivalent to 0.44 per cent.; average, 0.45 per cent. loss on drying. *Abbott brand:* A portion weighing 1.0009 gm. lost 0.1502 gm. on drying, equivalent to 15.01 per cent.; 1.0030 gm. lost 0.1529 gm., equivalent to 15.25 per cent.; average, 15.13 per cent. loss on drying. *Powers-Weightman-Rosengarten brand:* A portion weighing 1.0012 gm. lost 0.0041 gm., equivalent to 0.41 per cent.; 1.0023 gm. lost 0.0041 gm., equivalent to 0.41 per cent.; average 0.41 per cent. loss on drying. *Mallinckrodt brand* (second specimen): A portion weighing 0.5042 gm. lost 0.0023 gm., equivalent to 0.46 per cent.; 0.5023 gm. lost 0.0021 gm., equivalent to 0.0042 per cent.; average, 0.44 per cent. loss on drying. *Abbott brand* (second specimen): A portion weighing 0.5102 gm. lost 0.0098 gm., equivalent to 1.92 per cent.; 0.5193 gm. lost 0.0101 gm., equivalent to 1.94 per cent.; average, 1.93 per cent. loss on drying.

CALCIUM SULPHATE:—Portions of the material were ignited in an open crucible, first very cautiously with a small flame and afterward at a moderate red heat until constant weight was obtained. In order that any calcium sulphid that may have been formed by reduction with the heated carbon during the earlier stages of the ignition should be oxidized to calcium sulphate, the contents of the crucible were gently agitated during the heating by rotating the crucible in the flame and by tapping it against a piece of asbestos board. It was suggested by several of the manufacturers that after a preliminary ignition the residue be moistened with sulphuric acid and the ignition then completed. By this treatment any calcium sulphid (or calcium oxid) would be converted into calcium sulphate and perfect combustion of all carbon would

be assured. This method had already been tried in the Association laboratory and had been found superfluous, it having been found that by very slow ignition with free access of air practically perfect oxidation could be obtained. While a very faint odor of hydrogen sulphid could be detected in some cases on the addition of diluted sulphuric acid to the ash the results by the acid treatment were not very materially affected. For example, residues weighing respectively 0.1773 gm., 0.1756 gm., 0.1791 gm. and 0.1551 gm., after the acid treatment weighed respectively, 0.1787 gm., 0.1747 gm., 0.1791 gm., and 0.1551 gm. Hofmann and Mostowitsch[6] have shown that calcium sulphate in presence of air begins to be converted into calcium oxid at temperatures above 1,200 C. and in presence of carbon monoxid is reduced to calcium sulphid at temperatures above 900 C. They have also found that when calcium sulphid is heated in dry air about 73 per cent. of the resultant product is calcium sulphate, the balance being calcium oxid. While calculations from these findings indicate that resultant weight of the mixed substances amounts to about 72.2 per cent. of the amount that should have been given had all of the calcium sulphid been converted into calcium sulphate, our experiments indicate that the loss from this source is insignificant since, if the temperature be properly regulated, calcium sulphid is formed during the ignition in traces only or not at all. While it is possible that results may be obtained more expeditiously by the employment of the acid method such advantage is more than offset by the dangers from loss by spattering, which latter are very considerable unless diluted acid be employed and the mixture brought to dryness on the water bath previous to final ignition. Final treatment of the weighed residue with diluted sulphuric acid, however, was adopted as a routine treatment and in every case in which hydrogen sulphid was evolved the mixture was evaporated, dried and reignited.

RESULTS.—*Mallinckrodt brand:* From 0.9984 gm. of the dried material 0.3513 gm. ash was obtained, equivalent to 35.17 per cent.; 0.9974 gm. of the dried material gave 0.3509 gm. ash, equivalent to 35.18 per cent.; average, 35.18 per cent. calcium sulphate. *Merck brand:* From 0.4982 gm. of the dried material 0.1760 gm. ash was obtained, equivalent to 35.33 per cent.; 0.5016 gm. of the dried material gave 0.1767 gm. ash, equivalent to 35.23 per cent.; average, 35.28 per cent. calcium sulphate. *Abbott brand:* From 0.4414 gm. of the dried material 0.1552 gm. ash was obtained, equivalent to 35.16 per cent.; 0.4568 gm. gave 0.1613 gm. ash, equivalent to 35.31 per cent.; average, 35.24 per cent. calcium sulphate. *Powers-Weightman-Rosengarten brand:* From 0.5013 gm. of the dried material 0.1775 gm. ash was obtained, equivalent to 35.41 per

6. Bull. Am. Inst. Min. Eng., 1909, p. 51; ibid., 1910, p. 917, *et seq.*

cent.: 0.5041 gm. gave 0.1786 gm. ash, equivalent to 35.43 per cent.: average, 35.42 per cent. calcium sulphate. *Mallinckrodt brand* (second specimen): From 0.5019 gm. of the dried material 0.1773 gm. ash was obtained, equivalent to 35.32 per cent.; 0.5002 gm. of the dried material gave 0.1756 gm. ash, equivalent to 35.16 per cent.: average, 35.24 per cent. calcium sulphate. *Abbott brand* (second specimen): From 0.4985 gm. of the dried material 0.1751 gm. ash was obtained, equivalent to 35.13 per cent.: 0.5092 gm. of the dried material gave 0.1791 gm. ash, equivalent to 35.17 per cent.: average, 35.15 per cent. calcium sulphate.

Phenol, Heavy Metals, Etc.: Tests for these substances were carried out as described above in the text of the laboratory contribution.

PART II.

REPORTS ABSTRACTED FROM THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

J. LAWRENCE HILL'S CONSUMPTION TREATMENT

(Abstracted from The Journal A. M. A., Jan. 14, 1911)

As an example of the many consumption cures, whose exploiters endow well known and commonly used drugs with wonderful virtues which they do not possess or who use preparations which are absolutely worthless in the cases treated, an exposé of the treatment of J. Lawrence Hill was published in THE JOURNAL, A. M. A., Jan. 14, 1911. The methods of exploitation of this "cure" including advertisements and follow up letters were exposed and discussed, and as a result of a chemical analysis carried out in the Association laboratory the following report was published:

A box labeled "Dr. J. Lawrence Hill's Rational $10 Three-Fold Treatment for Consumption, Asthma, Bronchitis, Catarrh and all Diseases of the Throat, Nose and Lungs," and containing several forms of medication, was submitted to the Association laboratory for examination. The "treatment" consisted of (1) a box of sealed elastic gelatin capsules, containing a liquid in which floated a pill, and labeled, "Dr. J. Lawrence Hill's Globules"; (2) a small box of pinkish tablets labeled "Dr. Hill's Systematic Wafers"; (3) a small box of chocolate-coated tablets—"Dr. Hill's Laxative Tablets"; (4) a collapsible tube of a white ointment or salve labeled "Dr. J. Lawrence Hill's Plasma"; (5) a small vial (less than 2 drams) containing a brown liquid and bearing on the label—"Dr. J. Lawrence Hill's Antiseptic and Germ Killing Ozonol"; (6) a black hard rubber inhaler, and (7) a small box containing a tuft of cotton.

The "Globules": These were opened and the liquid and pill examined separately. The pill after being freed from the liquid was treated with hydrochloric acid, resulting in an evolution of hydrogen with a characteristic odor, such as is given off on treating iron with hydrochloric acid. On triturating one of the pills and washing away the lighter insoluble matter, a residue of shining metallic scales remained, which, when dissolved in hydrochloric acid, emitted hydrogen gas as when the entire pill was treated. The resulting solution

responded to tests for iron. On extracting the pills, from an alkaline medium, with ether, a bitter white crystalline substance was obtained, which responded to general alkaloidal tests, viz., it yielded a brown precipitate with iodin solution. Further examination showed that the substance gave strong reactions for quinin and less distinct ones for strychnin. No arsenic or other metals were found. From the results of the tests made it was assumed that the pills were composed essentially of iron (metallic), quinin and strychnin. The liquid in the globules was oily and possessed an odor of guaiacol. It was partially soluble in alcohol and completely soluble in ether and in chloroform. Alcohol extraction of the oil left a light yellow oil, practically odorless and tasteless; the portion extracted with alcohol responded to tests for guaiacol. The liquid portion of the "globules" then appeared to be a solution of guaiacol, or guaiacol-like body, in some bland oil.

The "Systemic Wafers": These were practically completely soluble in water, yielding a slightly turbid solution. They were sweetish in taste and slowly soluble in the mouth, resembling milk sugar. Tests for milk sugar indicated its presence. Further examination indicated the absence of metallic constituents, such as arsenic, antimony, mercury, iron, manganese, zinc, magnesium or calcium. Tests for alkaloids indicated the absence of alkaloids, such as atropin, strychnin, etc., while tests for such substances as iodids, bromids and salicylates indicated their absence. From the examination it was concluded that the tablets were essentially milk sugar.

The "Laxative Tablets": These were found to contain a substance having a faint, peculiar odor and a very bitter taste. Tests for arsenic and other heavy metals indicated their absence, and the tablets did not respond to tests for alkaloids. The bitter taste and the use for which the tablets were intended, pointed to the possible presence of aloin or aloes, and appropriate tests proved that aloin or aloes and a small quantity of starch were present. From the tests made, it was assumed that the tablets were principally aloes or aloin with some starch.

The "Plasma": This substance was found to be a white ointment or salve with a strong odor of oil of wintergreen. When subjected to steam distillation the distallate was found to contain material having the odor of wintergreen, while the residue in the distillation flask possessed an odor resembling oil of cloves. The "plasma" when extracted with ether yielded a substance which had the properties of stearic acid and the portion soluble in water had the properties of a stearic acid soap. The substance also contained a small quantity of a gummy substance resembling tragacanth. Tests indicated the absence of metals and alkaloids. It was concluded that the "plasma" was essentially a stearic acid ointment containing as

its chief ingredient oil of wintergreen and small quantities of other oils.

"Ozonol": This liquid possessed an aromatic odor and was soluble in alcohol, ether and in chloroform, but insoluble in water. When extracted successively with various solvents fractions were obtained which resembled such essential oils as sassafras, peppermint and eucalyptus. No alkaloids or other potent drugs were found. From the above properties "Ozonol" was assumed to be a mixture of aromatic oils resembling sassafras, peppermint and eucalyptus.

THE CHEMICAL EXAMINATION OF FORMUROL

Formurol, a product of the Chemische Fabrik Falkenberg, Falkenberg, Germany, was submitted to the Council on Pharmacy and Chemistry as "hexamethylentetramin-sodium-citrate," having the composition "$C_6H_7O_7Na.C_6H_{12}N_4$." Zernik (Arb. a. d. Pharm. Inst. d. Univ. Berlin, 1907, iv, p. 46) having found formurol, as sold in Europe, to be a mixture rather than a definite chemical compound, as claimed—it was considered important to examine the product as sold in this country and determine its true nature, since there was a possibility of its being a definite compound. The following report of the Association laboratory appeared as a part of the Council report (THE JOURNAL, Jan. 21, 1911):

Furmurol, Citrocoll and Aspirophen were submitted to the Council by the Cellarius Company of San Francisco. The manufacturers having failed to substantiate the claims they make for these products, the Council has voted that the preparations be refused recognition. The Council also authorized the publication of the following report, which deals particularly with one of the preparations—Furmurol.

W. A. PUCKNER, Secretary.

Formurol is the product of the Chemische Fabrik Falkenberg, Falkenberg-Gruenau, near Berlin, Germany. The Cellarius Company, San Francisco, acting as selling agents for the United States, submitted Formurol (along with Aspirophen and Citrocoll, also made by the same firm) to the Council, with the statement that it is "hexamethylentetramin-sodium-citrate," and that it has the following composition: "$C_6H_7O_7NaC_6H_{12}N_4$."

Zernik,[1] who examined these products, reported that Aspirophen, Citrocoll and Formurol do not have the composition that is claimed for them by the Fabrik Falkenberg. Formurol,

1. Arb. a. d. Pharm. Inst. d. Univ., Berlin, 1907, iv, p. 46.

he states, is not a definite chemical compound, but a mixture of hexamethylenamin and sodium citrate. The agents were advised of this fact by the Council and were asked to submit evidence to substantiate their claims. No such evidence was submitted.

Since a compound having the composition that is claimed for Formurol is theoretically possible, the Council requested that the product be examined in the Association Laboratory to determine whether it still was the simple mixture reported by Zernik, or whether, perhaps, it now possessed the formula claimed for it. The following report was made by the Association chemists:

> Formurol, as submitted to the Council, was in the form of tablets weighing about 1 gm. each and appeared to be composed of a fine white substance interspersed with some transparent particles. The tablets were readily soluble in water, were odorless and possessed a slightly acid taste. The aqueous solution responded to tests for hexamethylenamin, citrate and sodium. To determine whether hexamethylenamin was present in the free or the combined state, the method of Zernik was employed. This consists in the extraction of Formurol with chloroform, which dissolves out hexamethylenamin, leaving insoluble sodium citrate. As the use of the solvent, chloroform, would seem to preclude decomposition of such a hypothetical compound as "hexamethylenamin-sodium-citrate," the extraction of hexamethylenamin from formurol may be taken to demonstrate its presence in the free state.
>
> That Formurol is not a compound of hexamethylenamin, but a mixture of hexamethylenamin and sodium citrate, was further indicated by the appearance of the crushed tablets described above. Further, under the low-power microscope the powder was found to be composed of transparent crystals and white opaque particles which appeared to be masses of minute crystals. When treated with chloroform the transparent crystals dissolved, leaving the white masses intact, demonstrating the presence of two distinct substances, one soluble and the other insoluble in chloroform. It having been demonstrated that the residue obtained by evaporation of chloroform could not be weighed as hexamethylenamin, due to enclosed chloroform, the amount of this substance in the residue was determined.
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> The method used has been described in the Report of the Chemical Laboratory of the American Medical Association, Vol. I, p. 55, and depends on the decomposition of hexamethylenamin by means of sulphuric acid to form ammonium sulphate and formaldehyd. From this solution

the ammonia is liberated, distilled and determined[2] by titration and from the ammonia found the amount of hexamethylenamin is calculated. By this method Formurol was found to contain (a) 35.42 per cent. and (b) 35.32 per cent., or an average of 35.37 per cent. hexamethylenamin. The residue insoluble in chloroform was shown to consist essentially of disodium hydrogen citrate by determining[3] the amount of sodium (Na) contained in Formurol. The percentage of sodium calculated from the amount of sodium sulphate found was (a) 11.38 per cent., and (b) 11.20 per cent., or an average of 11.29 per cent., equivalent to 62.50 per cent. disodium hydrogen citrate.

As a check on this determination, the amount of material contained in Formurol which is insoluble in chloroform was determined.[4] It was found to be (a) 63.23 per cent. and (b) 63.49 per cent., making an average of 63.36 per cent., and thus agreeing fairly well with the results obtained when the sodium content was assumed to be disodium hydrogen citrate. From this analysis it appears that Formurol is not a definite compound of hexamethylenamin and sodium citrate, but instead is a mixture of these substances consisting approximately of hexamethylenamin 35.37 per cent. and sodium acid citrate (disodium hydrogen citrate) 63.36 per cent., practically a mixture of 1 part hexamethylenamin and 2 parts sodium acid citrate. These results agree with those reported by Zernik and show that the product now, as then, is not true to claims.

EDITORIAL NOTE: This report illustrates once more the value of the Council on Pharmacy and Chemistry and the Chemical Laboratory to the medical profession. Before the

2. Determinations were made, following the details of the method described in the report of the Chemical Laboratory of the American Medical Association, Vol. I, p. 55, with the following results: (*a*) 1.0769 gm. Formurol yielded an amount of ammonia requiring 10.96 c.c. normal sulphuric acid for neutralization, indicating the presence of 0.3815 gm. or 35.42 per cent. hexamethylenamin. (*b*) 1.1178 gm. Formurol required 11.36 c.c. normal sulphuric acid, equivalent to 0.3952 gm. or 35.32 per cent. hexamethylenamin, making an average of 35.37 per cent.

3. Sodium was estimated by converting to sodium sulphate in the usual way, with the following results: (*a*) 1.0319 gm. Formurol yielded 0.3621 gm. sodium sulphate, equivalent to 11.38 per cent. sodium. (*b*) 0.8783 gm. Formurol yielded 0.3035 gm. sodium sulphate, equivalent to 11.20 per cent. sodium; average 11.29 per cent., equivalent to 62.50 per cent. disodium citrate $C_6H_6O_7Na_2 + H_2O$.

4. The matter insoluble in chloroform was determined by weighing Formurol to a tared filter, which had been washed with chloroform and dried at 100 degrees, and percolating with chloroform till the dried filter and contents became constant in weight. By this method (*a*) 1.0769 gm. Formurol yielded 0.6826 gm. or 63.23 per cent. matter insoluble in chloroform; and (*b*) 1.1178 gm. Formurol yielded 0.7079 gm. or 63.49 per cent. insoluble matter; average, 63.36 per cent.

5. Therap. d. Gegenw., February, 1909.

Council was organized there was no agency to protect the physician's interests in the matter of pharmaceuticals. Under the old régime Formurol would have been heralded as a new "synthetic" of the most approved made-in-Germany type—and the claims would have gone unchallenged. To day its status is made clear and the profession is informed. Only those who have closely studied the question can realize what a wonderful power for commercial probity the Council has proved. Under the *laissez faire* system of the past, many large pharmaceutical firms gave little attention to the accuracy of the claims made for their products. If the advertising gave good "pulling" results, that was all that was asked or expected. Within the past five years a wonderful change has taken place in this regard and firms of the better class have so modified their advertising as to make it not only conservative in tone, but to approximate scientific accuracy.

THE INCOMPATIBILITY OF ANTIPYRIN, CALOMEL AND SODIUM BICARBONATE

(Reprinted, with additions, from The Journal A. M. A., Jan. 28, 1911, p. 287.)

An inquiry has been received from a correspondent concerning the incompatibility (thought to be dangerous) of a mixture of antipyrin, calomel and sodium bicarbonate in the following prescription:

℞ Mild mercurous chlorid ..... 2 grains
Antipyrin ..... 6 grains
Sodium bicarbonate ..... q. s.
Mix and divide into 12 powders.

On account of lack of authoritative information on the subject the matter was referred to the Association laboratory, which made the following report:

"The literature contains little definite information concerning the incompatibility of a mixture of these substances.

"Holland[1] states that antipyrin is incompatible with many substances, among which calomel and sodium bicarbonate are mentioned, but nothing is said concerning its incompatibility with a mixture of the two salts. Another writer[2] reports that antipyrin is incompatible with the chlorids of mercury, while another[3] declares that 'antipyrin is almost universally incompatible.' It is frequently stated that antipyrin is incompatible

1. Med. Chem., Ed. 2, 1908, p. 482.
2. Stark: Am. Pharm. Assn. Proc., 1893, xli, 506.
3. Fantus: Prescription Writing, 1906, p. 219.

with calomel, mercuric chlorid, mercurous oxid and metallic mercury being formed. This assertion, which is made by Werner[4], needs experimental confirmation. One writer[5] says that there is but little danger in dispensing calomel and antipyrin when the former is prescribed in small doses, as but a small part of the calomel (one-tenth or less) is converted into corrosive sublimate.

"As it seemed worth while to obtain some experimental data on the point involved, a mixture was prepared having the following composition:

Calomel	2 parts
Antipyrin	6 parts
Sodium bicarbonate	12 parts

"By qualitative tests it was demonstrated that when this mixture is treated with water a bluish-gray residue remains undissolved and a soluble mercury salt is found in solution. The composition of the insoluble residue was not determined, but there was considerable evidence that it is largely composed of metallic mercury and unchanged calomel. If the prescription powder be treated with an excess of 0.2 per cent. hydrochloric acid the reaction noted above does not occur: no mercury is found in solution and the calomel appears to be unchanged. If a mixture of calomel and antipyrin be suspended in water no reaction appears to take place at once. The calomel retains its natural color and no mercury salt is found in the solution. If to this aqueous solution of antipyrin containing suspended calomel some sodium bicarbonate be added the calomel immediately changes color and the mixture becomes of the same appearance as does the original mixture when treated with water.

"Preliminary determinations indicated that from one-sixth to one-fourth of the calomel present is converted into a soluble mercury salt. If the entire quantity prescribed be administered the patient would receive a soluble mercury salt equivalent to from ⅓ to ½ grain of corrosive sublimate.

"The incompatibility of the mixture will be apparent to any physician who will take the trouble to pour a few drams of water on a small portion of the powder; and that it is dangerously incompatible is shown by the large proportion of the mercury salt which is rendered soluble. If the mixture be administered in a capsule the danger would be lessened somewhat, as the acidity of the stomach would tend to neutralize the sodium bicarbonate, on the presence of which the reaction

4. Pharm. Ztg., 1896, xli, 395.
5. Critic and Guide, 1910, xiii, 117.

appears to depend. Since medical and pharmaceutical textbooks contain so little definite information concerning the incompatibility of this combination, too much blame should not be attached to those who have prescribed it and to pharmacists who have filled such prescriptions. However, if used at all, it should be in the most cautious dosage."

Details of Analysis

A mixture was prepared consisting of the following:

Mercurous chlorid	2 grains
Antipyrin	6 grains
Sodium bicarbonate	12 grains

On treating this mixture with water a bluish-gray residue remained undissolved and the presence of a mercury salt in the filtrate was demonstrated by the usual qualitative tests. The presence in the insoluble residue of metallic mercury and of unchanged calomel was shown by the usual tests.

After these preliminary tests were completed a mixture was prepared as follows:

Mercurous chlorid	20.00 grams
Antipyrin	60.00 grams
Sodium bicarbonate	120.00 grams

The several ingredients were carefully mixed, and weighed portions of the mixture treated with water under varying conditions.

To 1 gm. of the material 100 c.c. water were added and the mixture agitated. After standing over night the mixture was filtered, the filtrate warmed and saturated with hydrogen sulphid. The precipitate was collected in a tared Gooch crucible, washed with hot water, alcohol and carbon disulphid in the order named, dried at 100 C. and weighed. From 1 gm. of the material 0.0244 gm. mercuric sulphid was obtained, equivalent to 0.02476 gm. mercurous chlorid or 24.76 per cent. of the amount originally present. A duplicate of 1 gm. gave 0.0230 gm. mercuric sulphid, equivalent to 0.02333 gm. mercurous chlorid, or 23.33 per cent. of the amount present in the original mixture. The average percentage of the mercurous salt originally present which is rendered soluble is 24.05.

Five gm. of the mixture were treated with 100 c.c. water and the mixture allowed to stand over night. From one experiment 0.0883 gm. mercuric sulphid was obtained, equivalent to 0.08958 gm. mercurous chlorid, or 17.92 per cent. of the amount originally present. A duplicate gave 0.0922 gm. mercuric sulphid, equivalent to 0.09356 gm. mercurous chlorid or 18.71

per cent. of the amount originally present. The average percentage of the mercurous salt originally present which is rendered soluble is 18.32.

Ten gm. of the powder were treated with 250 c.c. of water and the mixture allowed to stand over night. From the filtrate from this 0.1682 gm. mercuric sulphid was obtained, equivalent to 0.17065 gm. mercurous chlorid, or 17.06 per cent. of the amount originally present.

As satisfactory results could not be obtained by this method the latter was varied in several particulars. As may be seen sufficient tests were made to demonstrate that a considerable proportion (1-6 to 1-4) of the calomel is rendered soluble.

Ten gm. of the powder were treated with 250 c.c. of water and the mixture allowed to stand 10 days at ordinary temperature with occasional agitation. From the filtrate obtained, from this 0.0829 gm. mercuric sulphid was obtained, equivalent to 0.0841 gm. mercurous chlorid or 8.41 per cent. of the amount originally present.

Five gm. of the powder were treated with 100 c.c. of water which had been saturated with carbon dioxid at ordinary pressure. A slow stream of carbon dioxid was passed through the mixture for sixteen hours, after which it was filtered and the filtrate treated with hydrogen sulphid. The precipitate of mercuric sulphid was collected with the usual precautions, dried and weighed. One sample of 5 gm. gave 0.0616 gm. mercuric sulphid, equivalent to 0.0625 gm. mercurous chlorid, or 12.5 per cent. of the amount originally present. Another sample gave 0.0468 gm. mercuric sulphid equivalent to 0.04748 gm. mercurous chlorid, or 9.50 per cent. of the amount originally present. Ten gm. of the mixture gave 0.0616 gm. mercuric sulphid, equivalent to 0.0625 gm. mercurous chlorid, or 12.66 per cent. of the amount originally present. A duplicate gave 0.0961 gm. mercuric sulphid, equivalent to 0.0975 gm. mercurous chlorid, or 9.75 per cent. of the amount originally present. The failure to obtain duplicate results would appear to show that the reaction is materially influenced by slight variations in the conditions of the experiment. As the experiments had accomplished their purpose—to demonstrate that the mixture was a dangerous one—no attempts were made at this time to further elucidate the reaction.

MRS. PRICE'S CANNING COMPOUND

(Reprinted, with additions, from The Journal A. M. A., Feb. 25, 1911, p. 607.)

When the federal Food and Drugs Act went into effect, the use of certain chemical preservatives which had been proved injurious was prohibited in food-stuffs that entered into interstate commerce. One of these preservatives was boric acid. As the harmfulness of this chemical became generally known, housewives and others who had been in the habit of using it for preservative purposes abandoned it. It was then that unscrupulous exploiters of chemical preservatives took a leaf out of the note-book of "patent medicine" fakers and put on the market, under fanciful names, preserving compounds composed largely of boric acid, but giving no indication of the presence of this chemical.

Mrs. Price's Canning Compound is sold on the claim that it will "prevent canned fruits and vegetables from souring and spoiling" and that it "may be used in canning all kinds of fruits" and "in making catsup, sweet pickles or anything that is liable to ferment." The Kansas State Board of Health has published at different times the results of two independent analyses of this "compound." These indicated that the stuff varied in composition. In view of this fact and because inquiries have been received, another analysis was made of Mrs. Price's Canning Compound, in the Association laboratory. The report of the Association's chemists is as follows:

"Mrs. Price's Canning Compound, manufactured by the Price Compound Company, Minneapolis, Minn., as received in the Association laboratory, was contained in an envelope bearing the name of the preparation, the name and address of the manufacturer and directions for its use.

"The envelope contained about 30 gm. of a white powder, soluble in water, possessing a salty taste and having an odor of benzoic acid. Qualitative tests indicated the presence of borate, chlorid, benzoate and sodium. Further experiments and the quantitative estimations indicated that the constituents found existed as boric acid, sodium chlorid and benzoic acid (possibly in part as benzoate) corresponding to the following amounts:

Boric acid, 94.74 per cent.
Sodium chlorid, 4.71 per cent.
Benzoic acid (calculated from total benzoate), 0.40 per cent.

"While the first analysis (Bulletin Kansas State Board of Health, October, 1909, p. 267) showed that the preparation consisted entirely of commercial boric acid, the second examination (Bulletin Kansas State Board of Health, November,

1909, p. 282) showed that about 6 per cent. of the boric acid had been replaced by sodium chlorid. The present analysis shows that the composition has been again altered by the addition of a small amount of benzoic acid. For all practical purposes, these changes are unessential. The variability is evidently the result of carelessness in the manufacture or it is made with the idea of misleading and confusing."

The housewife who uses this mixture does so, of course, not knowing that the chemical she is putting into her food has been declared injurious as a food preservative by the federal government. Neither does she realize that she is paying for what is essentially boric acid, worth 15 cents a pound, at the rate of $1.60 a pound.

ANALYTICAL DETAILS

Mrs. Price's Canning Compound as received in the Association laboratory is a white water-soluble powder, unctuous to the touch, possessing a salty taste, an odor of benzoic acid and yields a solution neutral to methyl orange but acid to phenolphthalein. Appropriate qualitative tests indicated the presence of sodium, borate, chlorid and benzoate, further experiments indicating the absence of appreciable quantities of other substances. With these constituents present there was a possibility of the borate being present as free boric acid, sodium borate or a mixture of both; the sodium being present as sodium benzoate or a mixture of two or more of these substances; and the benzoate being present as free benzoic acid, sodium benzoate or both. From the nature of the substance and from previous analyses the first combination of constituents that suggested itself, was boric acid, sodium chlorid and benzoic acid. Accordingly the results of the borate determinations were calculated to boric acid, the chlorid estimation to sodium chlorid and the benzoate determination to benzoic acid. The following are the results of the quantitative determinations:

Boric Acid: The method of Thomson (Sutton, Ed. 1896, page 92) was used to estimate the boric acid with the following results: (a) 1.2674 gm. of the "Canning Compound" required 19.35 c.c. normal sodium hydroxid solution, equivalent to 1.2000 gm. or 94.69 per cent. boric acid; (b) 0.8657 gm. of the compound required 13.23 c.c. normal alkali, equivalent to 0.8208 gm. or 94.79 per cent. boric acid; average, 94.74 per cent.

Sodium Chlorid: The chlorid content was estimated gravimetrically as silver chlorid, and calculated to sodium chlorid: (a) 1.6763 gm. material yielded 0.1924 gm. silver chlorid, equivalent to 0.0785 gm. sodium chlorid or 4.66 per cent.; (b) 1.4866 gm. material yielded 0.1741 gm. silver chlorid, equivalent to 0.0708 gm., or 4.77 per cent. sodium chlorid; average, 4.71 per cent.

Benzoic Acid: To determine the total, free and combined, benzoic acid the powder was dissolved in water, the solution acidified and the liberated benzoic acid removed by repeated extraction with large quantities of chloroform, the chloroform allowed to evaporate spontaneously, the residue dissolved in alcohol, phenolphthalein added and the solution titrated with tenth-normal potassium hydroxid. By this method the following results were obtained (a) 1.6490 gm. "compound" yielded a quantity of benzoic acid requiring 0.50 c.c. tenth-normal potassium hydroxid, equivalent to 0.0061 gm. benzoic acid or 0.38 per cent. of the material taken; (b) 1.8280 gm. "compound" required 0.60 c.c., equivalent to 0.0076 gm. benzoic acid or 0.42 per cent.; average, 0.40 per cent., representing the total, free and combined, benzoic acid.

While the sum of the percentages thus found—amounting to 99.85 per cent.—was considered ample evidence that the above assumed combination was correct—at least in so far as the borate and chlorid are concerned—the form in which the benzoate was present was still in doubt. Accordingly further experiments were made. As boric acid, sodium chlorid and sodium benzoate are practically insoluble in chloroform, percolation of the dry mixture with chloroform should remove any free benzoic acid present. The presence of free benzoic having been qualitatively demonstrated by this procedure, it was quantitively estimated, after isolation by percolation, by the method used in the total benzoate estimation. As a check, the extracted material was transferred to a separating funnel, dissolved in water, acidified and again extracted with chloroform; the quantity of benzoic acid thus obtained was the residual benzoic acid not removed by direct extraction with chloroform and probably in the form of sodium benzoate. By this procedure the following results were obtained:

(a) 3.6010 gm. of the preparation, when percolated with chloroform yielded a quantity of benzoic acid which required 0.50 c.c. tenth-normal potassium hydroxid, equivalent to 0.0061 gm. or 0.17 per cent. benzoic acid. (a-1) The extracted material when dissolved in water, the solution acidified and extracted as above outlined, yielded a quantity of benzoic acid requiring 0.69 c.c. tenth-normal potassium hydroxid, equivalent to 0.0085 gm. or 0.23 per cent. benzoic acid, making a total of 0.41 per cent. benzoic acid in the free and combined state.

(b) 3.5616 gm. material, percolated with chloroform, yielded a quantity of benzoic acid requiring 0.63 c.c. tenth-normal potassium hydroxid, equivalent to 0.0076 gm. or 0.21 per cent. benzoic acid. (b-1) The percolated material treated as above, yielded a quantity of benzoic acid requiring 0.53 c.c. tenth-normal potassium hydroxid, equivalent to 0.0065 gm. or 0.19 per cent. benzoic acid, making a total of 0.40 per cent. benzoic acid, free and combined.

These results would seem to show that the benzoate is present, in part, as free benzoic acid and, in part, in combination, hence it is reported as "Benzoic acid 0.40 per cent. (calculated from total benzoate)."

PLANTOXINE

(Reprinted, with additions, from The Journal A. M. A., March 4, 1911, p. 685)

A correspondent sent a specimen of a nostrum called Plantoxine to the Association laboratory, stating that it was sold for the treatment of hay fever, and that consequently he suspected it to contain cocain. This specimen was examined cursorily. Some time later an original package of Plantoxine was examined in greater detail and the following report published:

LABORATORY REPORT

"The specimen received was a white, odorless powder having the physical properties of milk sugar. Qualitative tests demonstrated the absence of cocain and other alkaloids and indicated that the substance was probably milk sugar. Some time later the correspondent, who had first written to the laboratory, sent an original package of Plantoxine for examination.

"Plantoxine is sold in packages each containing 40 powders, each powder containing about 2 grams (30 grains) of the preparation. The package, which retails for $1.00, contains about 2¾ ounces of the preparation.

"Quantitative examination indicated that Plantoxine consists entirely of milk sugar. The presence of medicinal substances could not be determined. If present their quantities must be small.

"In this connection it should be pointed out that the effect of cocain or its substitutes on the tongue furnishes a very sensitive and fairly distinctive test which may be used by physicians with advantage. If a trace of a powder, such as this, produces no benumbing effect when placed on the tongue the practical absence of cocain or its substitutes may be assured."

Details of Analysis

The absence of cocain and other alkaloids was demonstrated by the usual tests. The physical and chemical properties of the substance were like milk sugar. Lactose was determined by the A. O. A. C. method (Bur. Chem. Bull., 107, p. 48), the amount of copper reduced being calculated from the weight of cuprous oxid obtained.

Results: Two gm. of the material were dissolved in water and the solution diluted to 500 c.c. Four portions of 100 c.c. each of this solution gave, respectively, 0.3041, 0.3024, 0.3015 and 0.3024 gm. cuprous oxid, equivalent, respectively, to 100.15, 99.61, 99.40 and 99.61 per cent. of lactose in the specimen; average, 99.70 per cent. crystallized lactose.

Water: This was determined by drying at 130 C. One gm. lost 0.0526 gm., equivalent to 5.26 per cent.; 1.0009 gm. lost 0.0523 gm., equivalent to 5.23 per cent.; average, 5.24 per cent. Pure crystallized lactose contains 5.0 per cent. of water of hydration.

Ash: This was determined by ignition to constant weight. One gm. gave 0.0017 gm. ash, equivalent to 0.17 per cent.; 1.0009 gm. gave 0.0016 gm. ash, equivalent to 0.16 per cent.; average, 0.165 per cent. ash.

Control estimations by the above methods carried out on a laboratory specimen of commercial milk sugar gave 100.1 per cent. lactose, 5.64 per cent. water and 0.14 per cent. ash.

As a check on the results obtained for lactose by the laboratory, Mr. A. E. Paul, acting chief of the Chicago Food and Drug Inspection Laboratory, kindly consented to make a polariscopic examination of a portion of the specimen of Plantoxine. His report follows:

"The reading of a solution of one-quarter normal cane sugar strength (6.500 grams per 100 c.c.) in a 200 mm. tube, at 28 C. was 19.8° on the Ventzke Sugar Scale, which bears out your conclusion from chemical examination."

Similarity Between Nitrite and Acetanilid Poisoning

[Reprinted, with adaptations, from The Journal A. M. A., April 4, 1914, p. 1067.]

The following is an illustration of one of the many ways in which the Association's laboratory serves the profession:

A physician recently wrote that a preparation of liquor sodii phosphatus compositus, when administered to a patient, produced symptoms that simulated acetanilid poisoning. The sample sent in by the physician was examined by the Association chemists who reported:

"Tests which would detect minute quantities of acetanilid failed to reveal the slightest trace of this substance. The odor of the solution was distinctly characteristic of oxids of nitrogen such as are produced in the decomposition of nitrates or nitrites. The presence of a small quantity of nitrate—a regular constituent of this preparation—was detected and also the presence of considerable quantities of a nitrite.

Quantitative determinations showed the presence of an amount of nitrite equivalent to 2.9 per cent. sodium nitrite. It seems improbable that a nitrate used in the preparation of this mixture had decomposed to form a nitrite; it is more likely that a nitrite was used inadvertently. If this preparation was given in doses of 8 c.c. (2 fluidrams)—the U. S. P. dose for liquor sodii phosphatus compositus—the patient received 0.2331 gm. or three and one-half times the U. S. P. dose of sodium nitrite."

This note is published to point out the similarity between acetanilid and nitrite poisoning.

Analytical Details

From the correspondence above mentioned, the presence of acetanilid was expected, and accordingly, the solution under examination was extracted with ether, the ether extracts evaporated in a tared flask and the residue weighed. This procedure proved that not more than a trace of the material was soluble in ether, and hence was practically free from substances like acetanilid.

The odor of the solution, that of nitrogen oxids, pointed to the possible presence of a nitrite, which was then tested for and shown to be present by the following reactions: treated with a solution of antipyrin and dilute hydrochloric acid it yielded a green color; treated with a solution of potassium iodid and acid, free iodin was formed with liberation of nitric oxid gas; the solution reduced potassium permanganate solution. The presence of an apparently small quantity of nitrate was also found, but as the nitrite appeared to be present in much the larger proportions, the latter was estimated. The United States Pharmacopeia method of assay for spiritus etheris nitrosi was used with the following results: calculating the nitric oxid content to sodium nitrite, the most probable source of the nitrite: The solution under examination was diluted, 1 to 10 and 10 c.c. samples used, corresponding to 1 c.c. of the original solution.

Observed Volume.	Temperature.	Pressure Barometric.	Corrected Volume.
10.40 Cc.	23° C.	750.57 mm.	9.5 Cc.
10.10 Cc.	22° C.	751.58 mm.	9.40 Cc.

The average volume, 9.45 c.c., calculated to sodium nitrite is equivalent to 2.914 gm. per 100 c.c. of the original solution

BENETOL

(Reprinted, with additions, from The Journal A. M. A., April 15, 1911, p. 1128)

Benetol was first advertised to the medical profession with the claim that it was a glycerin-soap solution of alpha-naphthol. More recently it has been advertised to the laity with most extravagent and untruthful claims. In discussing the manufacturer's methods of exploiting Benetol, THE JOURNAL published the following concerning its composition:

In view of the claims that have been made for Benetol its composition is a matter of interest. What is this marvelous germicide; this "chemical," which destroys the germ of cancer; this wonderful discovery which "for six years Professor Carel toiled night and day" to produce; this potent typhoid destroyer, 10 drops of which in a gallon of infected water will make the water not only safe but beneficial; what is this new medical wonder? This inquiry was referred to the director of the Association's Chemical Laboratory and secretary of the Council on Pharmacy and Chemistry, who replied:

"Chemical examination of Benetol shows that it is a solution of alpha-naphthol containing about 18 gm. of the substance in 100 c.c. The solvent appears to consist of water, glycerin and soap. Alpha-naphthol is a well-known substance, closely related to, but not identical with, beta-naphthol which is official in the United States Pharmacopeia. The claim made in the advertising matter for Benetol, that it is a newly discovered compound is absurd. It is not a chemical compound but a simple solution of the well-known substance alpha-naphthol in the still better-known substances, glycerin, soap and water."

PAPINE

A Disguised Morphin Solution

(Abstracted from The Journal A. M. A., April 29, 1911, p. 1278)

Several inquiries having been received concerning the composition of Papine, the preparation was investigated in the Association laboratory, from which the following report was submitted:

For many years Papine has been advertised by its makers, Battle & Company, St. Louis, as an anodyne. In the circulars Papine is described in part as follows:

"Papine represents in pharmaceutical form the purely anodyne principles of opium free from the narcotic and tetanizing constituents."

"Papine is the anodyne or pain-relieving principle of opium, the narcotic and convulsive elements being eliminated. One fluid drachm is equal in anodyne power to one-eighth grain of morphin."

"Through special methods of preparation, the anodyne and analgesic principles of *Papaver somniferum* are so extracted as to free them of the narcotic and convulsive elements that ever have been, and must ever continue to be, serious objections to the use of opium and its common derivatives. . . . No demand is more regularly made on the physician than that for the relief of pain, and to be able to afford it promptly and completely, without the slightest deleterious action, is an advantage that cannot be overestimated."

"Unlike most derivatives and preparations of opium, Papine neither nauseates nor constipates; nor does it inhibit the secretory functions of the body."

"In conditions of extreme nervousness, especially in women, recourse to morphin is attended by the very real danger of the formation of a habit. Lastly, opium and its alkaloids must not be administered to persons whose kidneys are not in good working order on account of the risk of toxic accumulation."

"No such restriction exists in respect of Papine, its action being exerted exclusively on the element pain; in other words, it is purely anodyne."

"Papine does not nauseate, constipate nor create a habit."

From these statements the incautious physician might be led to infer that Papine is a preparation analogous or similar to the official tincture of deodorized opium. Formerly in the manufacture of the latter preparation, in addition to removal of the odorous substances, narcotin, then thought to be the principal convulsive 'alkaloid,' was also removed. By the process for the manufacture of this tincture, which is now official in the United States Pharmacopeia, most of the narcotine is found in the finished preparation. While it is a comparatively simple matter to remove the narcotin from opium and its preparations, thus eliminating most of the commonly reputed "convulsive elements,"[2] to remove the "narcotic elements" from opium would result in destroying the integrity of the product. The reasons for this are that morphin is the most powerfully narcotic substance found in opium, and it is present in the largest proportion of any of the alkaloidal constituents. Its removal from an opium preparation would, therefore, render that preparation practically valueless.

From Papine, however, the morphin has not been removed, for *since the passage of the Food and Drugs Act* the label has to admit that Papine contains 1 grain of morphin in each ounce!

A specimen of Papine was examined and found to be nothing more than a simple aqueous alcoholic solution of morphin containing glycerin. The preparation is flavored to imitate

1. Narcotin is now known to possess very little physiologic effect.

2. Of the opium alkaloids, laudanin and thebain possess the most powerfully tetanizing properties, but they are present in opium in too small quantities to produce any noticeable effect. Neither of these alkaloids is removed by the usual processes for "denarcotizing" opium.

cherry and colored with cochineal. With the exception of morphin, neither narcotin, codein nor other opianic alkaloids were found, while meconic acid, a characteristic constituent of opium, was absent. Since Papine is claimed not to cause constipation, and as is well known, this condition is frequently produced by morphin, it seemed possible that Papine might contain laxative substances. On examination, however, neither cascara, rhubarb, phenolphthalein nor laxative salts were found.

THE JOURNAL commented on the report as follows:

"While Battle & Co. have persistently exploited Papine as being an opium preparation having none of the objectionable qualities of opium, the analysis shows that the paradoxical claims made for it cannot be substantiated. In prescribing morphin there is an abundance of official preparations to choose from, and there certainly is no necessity or excuse for resorting to the much more expensive and in no way superior Papine."

Details of Analysis

Papine is a dark purplish liquid having a cherry-like odor and a sweetish taste. The specimen examined had a specific gravity at

$$\frac{25^\circ\,C.}{25^\circ\,C.} \text{ of } 1.0565.$$

Qualitative tests indicated the presence of morphin, ethyl alcohol, glycerin and cochineal. Small amounts of a chlorid and traces of a sulphate were present. Acetates, lactates and sugars were absent.

Opium Constituents. From the claims made for the preparation by the manufacturer, it might possibly be inferred that Papine is similar to the official tincture of deodorized opium. Accordingly, tests were made for opianic alkaloids other than morphin and for meconic acid. A portion of the specimen was dealcoholized, diluted with water and shaken with ether. The solvent was washed with water and portions evaporated. The residue from one portion of the solvent was very small; it was taken up in a small quantity of diluted hydrochloric acid and the solution filtered. On the addition of bromin to this solution, no precipitation took place, and on subsequent boiling the solution did not become rose-red. This was taken to indicate the absence of narcotin in Papine. The portion of dealcoholized Papine which had been shaken with ether was made alkaline with ammonia water and the mixture shaken with ether. The solvent was washed with water and shaken with diluted hydrochloric acid. The acid solution was made alkaline with ammonia, shaken with chloroform and the solvent evaporated. Only a very slight residue remained. This was subjected to the usual tests for codein, but with negative results.

A portion of the dealcoholized Papine was slightly acidified with hydrochloric acid and shaken with ether. The washed solvent was evaporated, the residue taken up with water and the solution treated with a drop of diluted ferric chlorid test solution. A red color was not produced. A portion of dealcoholized Papine was treated with a slight excess of lead acetate test solution, the precipitate washed with water, suspended in water and hydrogen sulphid passed in. The precipitated lead sulphid was removed by filtration, the filtrate evaporated to a small bulk and treated with ferric chlorid test solution. No red color was produced. These tests indicated the absence of meconic acid. No odor similar to opium was observed at any stage of the examination.

Laxative Substances.—A portion of the dealcoholized Papine was acidified with hydrochloric acid and shaken with ether. The washed solvent gave no red coloration on addition of ammonia water (absence of emodin and phenolphthalein). A small portion of the material was ignited. Only a trace of ash was given (absence of Epsom salts, Glauber's salt, etc.). These tests were taken to indicate the absence of the more common laxative substances.

Cochineal.—A portion of the dealcoholized specimen was slightly acidified with acetic acid shaken with amyl-alcohol, the solvent washed with water and shaken with a 1 per cent. solution of uranium nitrate. A deep green color was produced at once.

Chlorid.—Chlorid was determined as follows: Fifty c.c. were dealcoholized, diluted with 200 c.c. water, 10 c.c. nitric acid added, chlorid precipitated with silver nitrate, the precipitate collected, washed, dried, heated and weighed in the usual way. The results were calculated to crystallized morphin hydrochlorid ($C_{17}H_{19}NO_3$. $HCl + 3H_2O$) and to the equivalent of this salt in crystallized morphin ($C_{17}H_{19}NO_3 + H_2O$). From 50 c.c. of the solution 0.487 gm. silver chlorid was obtained; from a duplicate of 50 c.c. of the solution 0.481 gm. silver chlorid was obtained; average, 0.484 gm. silver chlorid. This is equivalent to 0.0968 gm. silver chlorid from each 100 c.c. of solution, or the equivalent of 0.2536 gm. crystallized morphin hydrochlorid in each 100 c.c. This quantity is equivalent to about 1.15 grain morphin hydrochlorid in each fluid ounce, or about 0.93 grain of crystallized morphin in each fluid ounce.

Since the label states that Papine contains 1 grain of morphin in each ounce, the findings from the chlorin determinations were taken to indicate that the morphin is present in the preparation combined as hydrochlorid.

THE CHEMICAL ANALYSIS OF TUBERCLECIDE

(Abstracted from The Journal A. M. A., May 13, 1911)

The results of a chemical examination of "Tuberclecide," manufactured by the "Tuberclecide Company" of Los Angeles, Cal., were summarized in THE JOURNAL of the American Med-

ical Association, May 13, 1911, p. 1109, as follows: "Examination of the contents of a sealed original bottle of Tuberclecide shows it to be essentially a solution of creosote or guaicol in some bland oil, probably olive oil."

This statement was based on the general properties of Tuberclecide and the results of the following analysis:

As received in the Association laboratory in an original sealed bottle, Tuberclecide was a light yellow oily liquid possessing the characteristic taste and empyreumatic odor of creosote or guaiacol.

As further evidence of the presence of these constituents the following tests, showing the presence of guaiacol as such or the guaiacol containing mixture creosote, were applied: A small quantity of Tuberclecide was extracted with alcohol, the alcohol separated from the oil and allowed to evaporate spontaneously. The evaporation of the alcohol left a residue consisting of a rather thick liquid possessing the odor and taste of creosote or guaiacol, and when ignited burning with a sooty luminous flame. Some of this liquid, as well as an aqueous extract of Tuberclecide, were both tested for creosote and guaiacol.

The liquid left on evaporation of the alcoholic extract responded to tests as follows: When shaken with an equal volume of petroleum benzine, then allowed to stand, the two liquids separated, a test which, according to the United States Pharmacopeia VIII, shows the absence of impurities in guaiacol. A small volume of the material heated with two volumes of sodium hydroxid test solution (U. S. P.) and cooled did not congeal. Pure guaiacol, according to the United States Pharmacopeia, should congeal under these conditions; thus this test indicates impure guaiacol. One part of the substance treated with ten parts concentrated sulphuric acid produced a yellow color changing quickly to reddish-brown. Pure guaiacol, according to the United States Pharmacopeia VIII, yields a pure yellow color, while creosote alone produces a red color, when tested in the same way.

Tests made on the aqueous extract of Tuberclecide yielded the following results: One drop of the aqueous extract treated with a drop of formaldehyd solution (1 to 1,000) and 1 c.c. concentrated sulphuric acid gave a violet color, rapidly changing to a dark turbidity. Pure guaiacol yields a clear violet color, while creosote alone yields a flocculent carmin turbidity. A solution of ferric chlorid added to the solution produced a dark bluish color, immediately changing to a muddy-brown

color. Guaiacol, according to the United States Pharmacopeia VIII, yields a violet color, turning green and finally yellow. The presence of creosote would mask the reaction for pure guaiacol, since, according to the United States Pharmacopeia VIII, creosote yields a violet color, changing to a muddy brown.

Inasmuch as creosote consists largely of guaiacol and inasmuch as these tests, though pointing to the presence of guaiacol, did not sharply distinguish from creosote, the report of the analysis was made to state that Tuberclecide contained ". . . creosote or guaiacol. . . ."

To determine the nature of the oil present, the saponification value of Tuberclecide was determined, according to the United States Pharmacopeia VIII. Side by side with this determination the usual blanks were made, as well as a check by heating a specimen of guaiacol with an equal quantity of the same alcoholic potassium hydroxid solution. The results obtained follow: (a) 1.2709 gm. Tuberclecide required 7.76 c.c. half normal potassium hydroxid, equivalent to a saponification value of 170.1; (b) 1.0111 gm. Tuberclecide required 6.36 c.c. half normal alkali, equivalent to a saponification value of 175.8; average of 172.9.

That the amount of alkali used in the saponification, represented only the oil in Tuberclecide and was not affected by the presence of guaiacol, was demonstrated by the fact that 25 c.c. of the alcoholic potassium hydroxids, requiring 11.58 c.c. normal acid for neutralization, required after heating with 1.2611 gm. guaiacol 11.55 c.c. normal acid for neutralization. The Halphen test for cotton-seed oil was applied and the result indicated the absence of this substance.

The oil had the general properties of olive oil. The guaiacol or creosote present would account for the saponification value of the mixture being somewhat lower than that of oils of the olive oil type.

THE ANALYSIS OF DEKOFA

A Caffein-Poor Coffee

(Abstracted, with additions, from The Journal A. M. A., July 1, 1911, p. 37.)

Recently a "decaffeinated" coffee, advertised and sold in this country by Merck & Co., first as "Dekafa" and now as "Dekofa," has attracted some attention, judging from the inquiries received regarding it. It is evident from these

inquiries that physicians in view of past experiences no longer rely on the unconfirmed statements of manufacturers, but require more convincing evidence than such statements before accepting the product for what it is sold. In view of the many inquiries regarding Dekofa, it was investigated and the following report published:

Dekofa is sold on the retail market in 1-pound packages labeled:

"Dekofa a genuine coffee from which the stimulating drug caffein has been largely removed. Particularly adapted for those to whom ordinary coffee is forbidden."

"Use precisely as ordinary coffee—no special directions for making are needed."

Besides the above the following statements, some addressed to the laity and others to the profession, are found in the advertising matter:

"Does the doctor forbid you coffee? Then ask him about Dekofa or Merck's 'Caffeinless' coffee. Most probably he'll let you drink that—and lots of it, too."

"Drink it at home and you won't have to drink it in Europe—and you may not have to go to Europe for your health, either."

"There is no need of you forbidding coffee to your patients troubled with 'heart' or 'nerve' or 'stomach' complaints, if you will direct them to use Dekofa, Merck's 'Caffeinless Coffee.'"

"The average caffein content of ordinary coffee is 1.3 per cent. Dekofa contains approximately 0.13 to 0.15 per cent. of caffein or about 10 per cent. only of the normal content."

From the standpoint of the chemist the claims made by the manufacturer bring up for discussion the following points: Dekofa is spoken of as "Merck's Caffeinless Coffee." This term would signify that the coffee is free from caffein, but as the firm makes a statement that the product contains 0.13 to 0.15 per cent. caffein, it is evident that here the manufacturers seek exemption from the truth under a sort of poetic license enjoyed in the past by "patent medicine" exploiters. The use of the phrase "caffeinless" can do but one thing—disguise the truth and hence should be dropped.

The firm asserts that "the average caffein content of ordinary coffee is 1.3 per cent." According to published analyses the caffein content of coffee varies from 0.64 per cent.[1] to 3.64 per cent.[2] This variation is due in part to natural causes and in part to the unsatisfactory methods of assay. Thus one investigator finds in coffee of different sources 0.64 to 1.53 per cent. caffein,[3] while three experimenters, working on

1. Arch. Pharm., 1876, p. 294.
2. Allg. Kaffee Zeitung, Rotterdam, from Proc. Amer. Pharm. Assn., 1885, p. 144.
3. Arch. Pharm., 1876, p. 294.

the same specimen of coffee, reported by the provisional method of the Official Agricultural Chemists, results ranging from 0.28 per cent. to 0.89 per cent. caffein and by another method from 1.02 per cent. to 1.21 per cent. caffein.

These results make it evident that no reliable average caffein content for coffee can be given, particularly when the method of assay is not defined. We are not in a position, however, to deny the correctness of the average caffein content of coffee as given by Merck & Co., nor, therefore, the claim that the presence of 0.13 per cent. caffein is an indication that 90 per cent. has been extracted. Assuming for the present that 0.13 per cent. caffein does not indicate the removal of 90 per cent., and in view of repeated inquiries it was decided to determine whether the actual caffein content of this product on the market agrees with the manufacturers' claims.

In the assay of Dekofa for caffein the modified provisional method of the Bureau of Chemistry, Department of Agriculture and the Görter method were used (U. S. Dept. Agriculture, Bureau of Chemistry, Bull. No. 132, p. 135). Using the provisional method the following results were obtained:

				Caffein by Nitrogen Estimation	
	——Per Cent. Crude Caffein——			Tenth-Normal	Per Cent.
Weight of Sample	First Extraction	Second Extraction	Total by Extraction	Acid Used	Caffein
10.5604	0.33	0.03	0.36	2.87	0.45
11.9751	0.12	0.13	0.25	4.21	0.47

The weight of the "crude caffein" which contains fatty and coloring matter from the coffee is seen to be somewhat higher than the caffein estimated by nitrogen, a difference also found in ordinary coffee, but accentuated in this case by the low caffein content.

It will be noticed in the first assay that the first extraction removed nearly all the caffein, while in the second case the caffein was nearly equally distributed between the two extractions. This difference is apparently due to the fact that the residue extracted in the first assay still contained some moisture, which appeared to favor the extraction, while in the second assay the residue was quite dry before being percolated. The final results, however, calculated from the nitrogen content, agree, showing that the difference in the "crude caffein" was not due to incomplete extraction of the caffein, but due rather to the presence of a greater or smaller amount of coloring matter, etc.

By the Görter, or direct extraction method, the following results were obtained:

Weight of Sample	Per Cent. Crude Caffein	Caffein by Nitrogen Estimation Tenth-Normal Acid Used	Per Cent. Caffein
9.7150	0.54	4.21	0.21
12.2700	0.60	6.61	0.25

By this method results were somewhat higher than those obtained by the provisional method. This was also the experience of those who compared the two methods.

From our experience with these two methods, the Görter method appears to be decidedly the most rapid and convenient, besides yielding higher results, indicating more complete extraction of the caffein.

THACHER'S WORM SYRUP

A Dangerous Santonin Mixture

(Abstracted, with additions, from The Journal A. M. A., July 15, 1911, p. 235)

The death of a child following the administration of several doses of a remedy called Thacher's Worm Syrup was reported to THE JOURNAL. The correspondent who did not see the patient until the fourth day after the ingestion of the first dose diagnosed the case as santonin poisoning and sent specimens of the preparation to the Association laboratory for examination.

Dr. Thacher's Worm Syrup is put on the market by the Thacher Medicine Co., Chattanooga, Tenn., under the following claims:

"Dr. Thacher's Worm Syrup is scientifically prepared from materials which are known to have a sure and safe effect on the child and to leave it in a healthy condition."

The preparation was examined and the following report was published in THE JOURNAL:

Unbroken packages of Thacher's Worm Syrup were obtained, and examined in the Association's laboratory to determine whether there was santonin in the product, and if so, in what quantity. The preparation comes in bottles containing a little more than 1½ fluid ounce (47 c.c.). It is a thick, dark-brown syrup having the odor of cloves and anise and a sweet, anise-like flavor. The preparation contains a noticeable amount of small, grayish crystals in suspension. These crystals were found by qualitative tests to be nearly pure santonin. Alkaloids were absent. The quantitative

examination indicated that the preparation contains about 1.14 gm. (18 grains) of santonin in each 100 c.c. (3⅓ fluid ounces), the greater proportion of this drug being in suspension. This means that each teaspoonful dose of the nostrum contains about ⅔ of a grain of santonin.

Details of Analysis

The absence of alkaloids having been demonstrated by the usual tests santonin was determined as follows: The specimen was well shaken. A measured quantity of the syrup was filtered through a tared Gooch crucible and the insoluble residue washed with cold water until the washings were free from sweet taste. The residue was then dried at 90 C. and weighed, the weight obtained representing the undissolved santonin in the syrup. The filtrate and washings were united, a few drops of diluted hydrochloric acid added, and the mixture extracted with ether until a portion of the solvent when evaporated no longer gave tests for santonin. The ethereal solutions were combined, washed twice with water and the ether removed by evaporation. The residue was dried at 90 C. and weighed, the weight obtained representing the dissolved santonin in the syrup. The absence of resins and fats in appreciable quantities from the ether soluble residue was demonstrated by the almost complete solubility of the dried residue in hot water.

The identity of the santonin was verified by the following tests: A portion was recrystallized once from hot water and its melting point taken. The specimen melted at 170°. The melting point for santonin given in the U. S. P. VIII is 170.3° C. About 0.01 gm. of the recrystallized substance was shaken with 2 c.c. of 70 per cent. sulphuric acid and the mixture heated to 100° C. On the addition of a trace of diluted ferric chlorid test solution a violet coloration resulted. A portion of the recrystallized material when heated with alcoholic potassium hydroxid gave a red color.

Results.— Twenty-five c.c. of the material gave 0.2333 gm. undissolved santonin and 0.0472 gm. dissolved santonin, equivalent to a total of 1.1220 gm. in 100 c.c. of the syrup. The contents of one bottle (the capacity of which was found to be 47 c.c.) gave 0.4563 gm. undissolved santonin and 0.0902 gm. dissolved santonin, equivalent to a total of 1.1630 gm. in 100 c.c. of the syrup. Average 1.142 gm. santonin in 100 c.c. of the syrup. This is equivalent to 5.2 grains of the drug in each fluid ounce, or about ⅔ grain in each fluid dram of the syrup.

THE ANALYSIS OF IODONUCLEOID

(*Reprinted, with additions, from The Journal A. M. A., July 22, 1911, p. 309*)

In reply to an inquiry regarding the preparation called iodonucleoid, the Association laboratory replied as follows:

This preparation was at one time considered for inclusion with New and Nonofficial Remedies, and at that time it was examined in this laboratory. The examination showed that iodonucleoid contains:

Phosphorus	0.79 per cent.
Calcium (Equal to 0.6 per cent. CaO).	0.43 per cent.
Iodin	24.2 per cent.

When 2 gm. was dissolved in tenth-normal potassium hydroxid volumetric solution and acetic acid added until faintly acid, an abundant, white, flocculent precipitate formed. This precipitate was collected, washed with water, transferred to a beaker, phenolphthalein added and tenth-normal potassium hydroxid volumetric solution run in until a pink color was produced. This required 15 c.c. of tenth-normal alkali. Subtracting from the 2 gm. of iodonucleoid the 24 per cent. iodin, leaves 1.52 gm.; this divided by the c.c. of alkali used indicates an equivalent weight of 1013.

Authorities differ widely regarding the amount of phosphorus contained in nuclein from different sources, the figures ranging from 2.9 per cent. to as high as 10 per cent. If the nuclein from which iodonucleoid purports to be made contained but 2.9 per cent. phosphorus, the preparation, after allowing for 24 per cent. iodin, should still contain 2.2 per cent. phosphorus instead of 0.79 per cent., as found by analysis. A true nuclein should contain no calcium. If iodonucleoid is a casein compound of iodin we might expect to find, if the casein had been freed from milk by acidulation without further purification, both calcium and phosphorus. The equivalent weight of casein is given by Long (Jour. Am. Chem. Soc., 1906, xxviii, 372) as 1124. This figure was obtained on a casein of high purity, and the figure of 1013 given above agrees fairly well with Long's figure for casein. The evidence, therefore, indicates that iodonucleoid is a compound of iodin and casein, and not a nuclein compound.

The findings of the laboratory were at that time submitted to Prof. John H. Long of Northwestern University, who said:

> "We have also made a number of examinations of iodonucleoid. We determined in it the iodin and found the amount 24.2 per cent. by weight, which is a little more than that claimed by the manufacturer. We have also tested the solubility of this substance and find it to

behave about as your laboratory did. As you know, we have been making a number of preparations from casein, and recently we have determined the combining power of casein with various acids, including hydriodic acid. This acid when evaporated in moderately strong solution with casein yields finally a hard, dry mass, which may be ground up to a powder resembling very closely the preparation under discussion. Various amounts of iodin may be combined here, depending on the strength of the iodin solution used, and we have secured some containing over 35 per cent. of iodin. Several of these preparations resemble closely iodonucleoid, so far as solubility, appearance and reaction with alkalies on titration are concerned. I am unable, therefore, to distinguish this preparation from the casein compounds which we are making."

From this it would appear that iodonucleoid is not a compound of nuclein, as indicated by the name, but instead is a casein compound of iodin.

Iodonucleoid, then, seems to be another one of the many iodin "substitutes" which have been put on the market. Other iodin substitutes are Iodalbin, manufactured by Parke, Davis & Co.; Iodipin, manufactured by E. Merck & Co., and Sajodin, manufactured by the Farbenfabriken of Elberfeld Co. As these products have been examined by the Council and found eligible for inclusion with New and Nonofficial Remedies, physicians who wish to use substitutes for potassium iodid would do well to use them instead of a product presented under a misleading name. Physicians should understand, however, that these organic iodin compounds are non-irritating because the iodin is held in such combination that it is much less active. It seems probable that they are therapeutically active only to the extent that the iodin content is dissociated from the organic compound and converted into ionic iodin. A discussion of a number of iodin substitutes is found in an article by von Notthafft (*Monatsh. f. Prakt. Dermat.*, Oct. 15, 1910, p. 343), which was abstracted and commented on in THE JOURNAL, March 4, 1911, p. 685.

Von Notthafft believes that the lower degree of toxicity which these remedies exhibit has its basis in a feebler activity; either the substitutes evolve too little iodin or they split it off with greater difficulty. Physicians should, therefore, view with some distrust the claims of manufacturers that their products are not only non-irritating, but at the same time possess unusual therapeutic efficiency. This will apply with especial force if there is any tendency to conceal the nature or origin of the combination.

EN-AR-CO OIL

A Poisonous Nostrum for Curing Rheumatism and Making Hens Lay

(Abstracted, with additions, from The Journal A. M. A., July 29, 1911, p. 407)

Inquiries having been received concerning the composition of a nostrum known as "En-Ar-Co Oil," an original package of the preparation was examined and the following report published:

Qualitative tests demonstrated the presence of ethyl alcohol, iso-amyl alcohol (the chief constituent of "fusel oil"), capsicum and a volatile oil of a greenish color and eucalyptus-like odor, but which was not identified. Neither cantharides nor ginger could be found and alkaloids were absent. While no exact separations were made it is concluded that about 90 per cent. of the preparation consists of "fusel oil."

From the results of this cursory examination it appears that a mixture of "fusel oil" and tincture of capsicum with a little oil of eucalyptus added would have properties similar to those of the "Wonderful Japanese Oil."

Details of Analysis

The specimen of En-Ar-Co Oil examined was of a dark, brownish color and had an odor like "fusel oil." A portion was distilled from an ordinary side-delivery distillation flask and the temperature at which the several fractions passed over noted. The following results were obtained from 50 c.c. of the material:

		Per Cent. by Volume
Between 87 and 90 C.	2 c.c.	4
Between 90 and 100 C.	4 c.c.	8
Between 100 and 120 C.	8 c.c.	16
Between 120 and 130 C.	20 c.c.	40
Between 130 and 140 C.	12 c.c.	24
Loss and residue (by difference)	4 c.c.	8

Water was added to the residue in the flask after distillation and the mixture distilled with steam. The distillate was shaken with ether and the solvent allowed to evaporate spontaneously. A pale green oil having an eucalyptus-like odor remained. This oil was not identified. The fractions which passed over between 120 C. and 140 C. were united, the mixture distilled and the fraction passing over between 128 C. and 132 C. collected separately.

Amyl-Alcohol.—The presence of 3-methyl butan-1-ol (iso-amyl alcohol, fermentation amyl alcohol) in the fraction boiling between 128 C. and 132 C. was demonstrated by the following tests:

A portion when warmed with twice its volume of concentrated sulphuric acid became of a deep red color.

Another portion when warmed with concentrated sulphuric acid and potassium dichromate gave a noticeable odor of valeric acid.

Another portion when warmed with concentrated sulphuric acid and sodium acetate gave a noticeable odor of amyl acetate. These tests together with the boiling point and odor of the fraction were taken to indicate the presence of iso amyl alcohol.

Capsicum.—The presence of capsicum was proved by treating a portion of the non-volatile residue (after steam distillation) by the method described by LaWall (Am. Jour. Pharm., 1909, lxxxi, 218). The method consists in saponifying an ether extract of the acidified preparation with alcoholic potassium hydroxid, removing the alcohol by evaporation, extracting the diluted residue with ether and tasting the residue after spontaneous evaporation of the solvent. A pungent taste indicates capsicum.

Cantharides. According to the following test the absence of cantharides was indicated: A portion of the specimen was tested by a method described by Lenz and Lucius (Apoth. Ztg., 1907, xxii, 578). The method consists in distilling the preparation with steam after acidification with phosphoric acid, shaking the distillate with chloroform and applying the residue obtained by spontaneous evaporation of the solvent to the skin of the forearm. If cantharides were present in appreciable amounts, redness, swelling and even blisters will appear on the arm after twenty-four hours. A portion of the specimen was evaporated on the water bath until most of the "fusel oil" was removed. The residue was then acidified and treated as indicated above. No redness or swelling appeared on the forearm after the chloroform extract had been applied and allowed to remain for twenty-four hours.

Ethyl Alcohol.—The first portions obtained in the fractional distillation were saturated with sodium chlorid and shaken with petroleum ether. The salt solution was drawn off, placed in a distillation apparatus, distilled, and the presence of ethyl alcohol in the distillate demonstrated by the usual tests.

Ginger.—This was tested for by Seeker's method (Bur. Chem. Cir. lxvi, p. 22). The method is carried out as follows:

Dilute 10 c.c. of the extract to 30 c.c., evaporate off 20 c.c., decant into separatory funnel, and extract with an equal

volume of ether. Evaporate the ether spontaneously in a porcelain dish and to the residue add 5 c.c. of 75 per cent. sulphuric acid and about 5 mg. of vanillin. Allow to stand for fifteen minutes and add an equal volume of water; in the presence of ginger extract an azure blue color develops.

The test as above described was carried out on 10 c.c. "En-Ar-Co Oil" with negative results. As a control the test was applied to 10 c.c. of an authentic tincture of ginger. The color produced may be described as a rich, violet-blue and was best observed after allowing the acid-vanillin mixture to stand over night. The test gave a positive result when applied to a mixture of 9 c.c. "En-Ar-Co Oil" and 1 c.c. tincture of ginger.

The negative results obtained by applying this test to the specimen and the absence of all odor and taste of ginger in the residues at various stages of the examination, were taken to indicate absence of preparations of this substance.

MAYR'S WONDERFUL STOMACH REMEDY

Another Fake Gall-Stone Remedy

(Reprinted, with additions, from The Journal A. M. A., Aug. 19, 1911, p. 674)

The fake "gall-stone trick" and "tapeworm trick" have long been worked by itinerant medical swindlers. As every physician knows, the administration of large doses of some bland oil such as olive oil, especially when followed by a saline cathartic, results in the passage of a number of greenish concretions from the bowels. The victim is made to believe that these concretions are gall-stones, and he feels that he is getting his money's worth in proportion to the number of these "stones" that are passed.

This method of defrauding the public is now being worked by "patent medicine" venders as well as by travelling fakers. In THE JOURNAL, Sept. 24, 1910, one of the most widely advertised of these fake gall-stone cures—"Fruitola"—was discussed. A number of inquiries have been received regarding the composition of another preparation of the same type, "Mayr's Wonderful Stomach Remedy," made by George H. Mayr, a Chicago druggist. One correspondent submitted a number of pseudo-gall-stones passed by one of his patients who had taken Mayr's nostrum. With the specimen the physician sent the following letter:

FIG. 1.—Photographic reproduction (actual size) of some of the supposed gall-stones passed by a victim who had taken Mayr's Wonderful Stomach Remedy. Anybody can perform the same trick by drinking a pint of olive oil and following it up with a seidlitz powder!

"The accompanying specimen was brought to me by a patient whom I have been treating for membranous colitis. One of her symptoms is pain in the left side of the abdomen. There have been no attacks of biliary colic nor has the physical examination afforded any data on which to base such a diagnosis. On the advice of a friend the patient had taken 'Mayr's Wonderful Stomach Remedy,' which appears to be similar to 'Fruitola' recently exposed by you. I have found on a superficial examination that the masses which closely resemble gall-stones consist of a soap, part of which is insoluble. I would like to know whether the base of the insoluble portion of the soap consists largely of magnesia. If so, is it probable that this base is furnished by the saline cathartic given after the remedy or is a sufficient amount of earthy base excreted by the intestine to cause the formation of so large an amount of these pseudo-calculi?"

To be able to answer this question intelligently, the Association's chemists analyzed not only the nostrum but also the "gall-stones." The laboratory report follows:

LABORATORY REPORT

"Mayr's Wonderful Stomach Remedy" consists of a bottle of oil and two powders contained in a red carton on which appears the following:

"Mayr's Wonderful Stomach Remedy for Stomach Troubles, Indigestion, Gases in the Stomach and Intestines, Dizziness and Fainting Spells, Colic Attacks, Torpid Liver, Constipation, Gastritis, Yellow Jaundice, Appendicitis, Gallstones, etc.

"The above ailments are mainly caused by the clogging of the intestinal tract with poisonous accretions—which are caused by a catarrhal condition of the gall-bladder and duct, liver, stomach and intestinal tract—backing up poisonous fluids into the stomach, and otherwise deranging the digestive system.

"This remedy painlessly removes these accretions without surgical operation, takes out inflammation from the entire intestinal tract and renders the same antiseptic."

A pamphlet comes with the bottle consisting chiefly of that sheet anchor of the patent medicine faker—testimonials. Of course fraudulent claims are made.

"Price $1.00 per bottle; worth $100.00."'

"A positive remedy for appendicitis."

"It is composed of nothing but strictly pure food vegetable ingredients."

"Unsurpassed for liver complaint."

"Those who believe that they have gallstones we implore you—*Don't submit to a dangerous surgical operation.* . . . The full course of Mayr's Wonderful Stomach Remedy not only painlessly removes this accretion, but allays the inflamed or catarrhal condition that causes them . . ."

The instructions for taking this nostrum directed the patient to take one powder at 3 o'clock in the afternoon; at bedtime the entire contents of the bottle (about a half-pint) was

to be taken at one dose. The next morning the second powder was to be taken. The patient was told:

"When the bowels operate use a vessel and note the poisonous secretions removed by this remedy, in some cases dark green or yellow lumps varying in size from a fine bead to an olive—in severe cases even larger. In other cases quantities of thick tenacious slime or mucous [*sic*]. These accumulations are weakening and poisonous."

The bottle contained about six ounces of a bland yellow oil, which from the results of analysis appeared to be olive oil.

Fig. 2.—A reduced photographic reproduction of a typical advertisement of this fake gallstone cure. From *Happy Hours*.

The powders, each of which weighed about one ounce, appeared to be ordinary Rochelle salts, one disguised by the addition of about 6 per cent. compound licorice powder and the other by the addition of about 4 per cent. powdered licorice root.

From the composition of the nostrum, as determined by analysis, it was expected that the concretions, which the physician had submitted for examination, would be found to consist of a sodium soap formed in the intestinal canal by the action

of the alkaline fluids on the fatty oil. As no magnesium was found in the preparation, the correspondent's suggestion that the "gall-stones" might be a magnesium soap did not appear plausible. Nevertheless it was thought worth while to demonstrate in a general way the composition of these masses.

The so-called gall-stones, weighing in the aggregate about 21 grams (315 grains) were grayish-green and of the size shown in the illustration (Fig. 1). When received they had the consistency of soft wax but on standing in the laboratory for several days, the material separated into a dark oily portion and an amorphous gray part. Analysis demonstrated the presence of both free and combined fatty acids as well as of considerable sodium and some potassium. Lack of material made it impossible to determine whether the combined fatty acids existed in combination with sodium or potassium or in the original condition as oil; for the same reason, it was impossible to determine in what form the sodium and potassium were present. As the amount of sodium found was in itself more than sufficient to account for all the combined fatty acids, it is probable that the masses consisted essentially of free fatty acids and soap (sodium salt of fatty acids).

In short, the so-called gall-stones are principally a mixture of fatty acids and soaps produced by the action of the alkaline intestinal fluids on the large amount of oil taken.

Details of Analysis

Analysis of the Nostrum: The oil had the general physical character of olive oil. Absence of cotton seed oil was shown by the Halphen reaction.

Powder No. 1, weighing 27.1303 gm., possessing a light cream color and a slight odor of fennel, was largely soluble in water leaving a small quantity of insoluble matter. The aqueous solution responded to tests for sodium, potassium and tartrate, while tests for heavy metals, magnesium, free acids, or carbonates indicated their absence. The taste of the powder was like that of Rochelle salts, with its characteristic cooling sensation on the tongue. These properties together with the qualitative composition as given above point to the presence of potassium and sodium tartrate.

The insoluble portion of the powder under the microscope was seen to consist almost entirely of vegetable structures, containing structures characteristic of licorice root and senna. Extraction with chloroform and evaporation of the chloroformic extract yielded crystals of sulphur. These properties, the presence of senna, licorice root, sulphur and an odor of fennel all point strongly to the presence of compound licorice powder. (Pulvis glycyrrhizæ compositus.)

To determine the content of potassium and sodium tartrate a weighed sample of the powder was charred, leached with hot water, the residue again charred and again leached, and

the combined aqueous extracts titrated with normal sulphuric acid, using methyl orange indicator. By this method (*a*) 1.3391 gm. powder required 8.77 c.c. normal sulphuric acid, equivalent to 1.2570 gm. or 93.85 per cent. potassium and sodium tartrate; and (*b*) 1.4737 gm. of the powder required 9.88 c.c. normal acid, equivalent to 1.3850 gm. or 93.95 per cent. potassium and sodium tartrate: an average of 93.90 per cent.

The amount of compound licorice powder present was calculated from the sulphur content of the powder. The latter was found by extracting with chloroform and evaporating the chloroform in a tared dish, drying and weighing the crystals. Thus (*a*) 1.6136 gm. powder yielded 0.0070 gm. or 0.47 per cent. sulphur; and (*b*) 1.7399 gm. powder yielded 0.0097 gm., or 0.55 per cent. sulphur, an average of 0.49 per cent. This content of sulphur calculated to compound licorice powder, corresponds to 6.12 per cent. of the latter.

Powder No. 2 had the same general properties of No. 1, excepting that it had an odor of licorice and contained no sulphur, and under the microscope no senna could be found, while the characteristic structures of licorice root were found. From these properties it was concluded that Powder No. 2 also contained Rochelle salts as its chief constituent, with a small quantity of powdered licorice root, instead of the compound licorice powder.

The quantitative determination of potassium and sodium tartrate was carried out as in Powder No. 1 and yielded the following results: (*a*) 1.6864 gm. powder required 11.49 c.c. normal acid, equivalent to 1.6100 gm. or 95.45 per cent. potassium and sodium tartrate; and (*b*) 2.0456 gm. required 13.96 c.c. normal acid, equivalent to 1.9550 gm. or 95.63 per cent. potassium and sodium tartrate; an average of 95.54 per cent.

The insoluble matter in the powder was determined by simply extracting with water and washing the insoluble matter on a weighed Gooch crucible, drying and weighing. This insoluble matter, from its characteristics was assumed to consist essentially, if not entirely, of powdered licorice root. The following results were obtained: (*a*) 1.5554 gm. powder yielded 0.0682 gm. or 4.38 per cent. insoluble material; and (*b*) 2.0454 gm. powder yielded 0.0774 gm. or 4.22 per cent. material; an average of 4.30 per cent.

ANALYSIS OF THE "GALL-STONES":—The specimen as submitted was mixed to a homogeneous mass, portions of which were then used in the following examination.

Treated with water the material yielded a turbid mixture showing the presence of some insoluble matter. With alcohol a much less turbid solution resulted, which was acid to phenolphthalein, indicating the presence of free acid.

Free Fatty Acids: To determine the free fatty acids weighed portions of the material were dissolved in 20 c.c.

alcohol, phenolphthalein added, titrated with tenth-normal alkali and subtracting the amount of alkali required to neutralize the alcohol used (determined in a blank experiment); thus (*a*) 0.8950 gm. material required 11.06 tenth-normal alkali for neutralization, or 12.35 c.c. per gm. of original material used; and (*b*) 0.6335 gm. required 7.86 c.c. tenth-normal alkali or 12.23 c.c. per gm. of material; an average of 12.29 c.c., which is equivalent to 34.43 per cent. fatty acid, calculated as oleic acid.

Total Fatty Acids: To determine total fatty acids weighed portions of the original material were treated with dilute sulphuric acid, whereby any fatty acid combined in the form of soap would be set free and then the acid so obtained, along with the free fatty acid, originally present, was extracted by shaking with repeated portions of chloroform. The chloroformic extract was collected in tared dishes, the chloroform allowed to evaporate, the residue dried over sulphuric acid in a dessicator and weighed. The material thus obtained was titrated as above and from the quantity of alkali used the total fatty acids were calculated as oleic acid. Following this method (*a*) 1.8317 gm. material yielded 1.3048 gm. residue, which required 45.47 c.c. tenth-normal alkali for neutralization, corresponding to 24.82 c.c. per gm. of original material taken; and (*b*) 0.7136 gm. substance yielded 0.5095 gm. of residue from chloroformic extraction, requiring 17.75 c.c. tenth-normal alkali, equivalent to 24.87 c.c. alkali per gm. of original material; an average of 24.84 c.c. tenth-normal alkali. This corresponds to 69.59 per cent. of total fatty acids, calculated as oleic acid.

Any oil contained in the specimen would by this method be extracted and weighed, but not titrated, with the total fatty acids. The absence or presence of oil was to be determined by taking the saponification number of the material; these experiments miscarried and because of lack of material could not be repeated. While agreement of weight with titration, at first glance, precludes the presence of substances other than fatty acid, as a matter of fact the residue, if it contained fatty acids having a lower molecular weight than oleic acid, might have also contained undecomposed oil and yet have required an amount of alkali which when calculated to oleic acid would have indicated an amount of the latter agreeing with the weight of the residue. Thus if in (*a*) the residue had consisted of 0.8499 gm. oleic acid, 0.2355 gm. palmitic acid and 0.2194 gm. oil the titration would still have required the same quantity of alkali, which would represent an amount of oleic acid equal to that above reported.

Ignition of some of the original material yielded an ash which responded to tests for sodium, potassium and traces of chlorid and sulphate. Other elements such as calcium, magnesium and the heavy metals were found to be absent.

The sodium and potassium were estimated by converting to the sulphates and weighing, then converting to chlorid, and estimating the potassium as the chlor-platinate, and from these results calculating the sodium content. Thus (a) 0.6670 gm. material yielded 0.0270 gm. combined sodium and potassium sulphates and this in turn yielded 0.0097 gm. potassium platinic chlorid, equivalent to 0.0033 gm. or 4.94 per cent. potassium calculated as the sulphate; and (b) 0.7653 gm. material yielded 0.0309 gm. sodium and potassium sulphate, which yielded 0.0106 gm. potassium platinic chlorid, equivalent to 0.0038 gm. or 4.96 per cent. potassium, calculated as the sulphate. From these figures the material was found to contain sodium equivalent to 35.47 per cent. sodium sulphate and potassium, equivalent to 4.92 per cent. potassium sulphate. All the fatty acid in combination calculated to sodium oleate is equal to 37.50 per cent. of the original material. This leaves considerable sodium and potassium unaccounted for, but the lack of material precluded a more complete investigation, as to the form in which the sodium and potassium existed.

JAROMA

A New, Euphonious Name for an Old, Ill-Smelling Drug

(Abstracted, with additions, from The Journal A. M. A., Sept. 2, 1911, p. 835)

About eighteen months ago the attention of THE JOURNAL was called to a preparation called "Jaroma," marketed by the Jaroma Company of New York City, and advertised to physicians as a specific for sleeplessness. The general tone of the reading matter indicated that Jaroma probably belonged to the same class of humbugs as Oleozone and Plantoxine. As the efforts of the promoters at that time appeared to be devoted more assiduously to the sale of Jaroma Company stock than to the exploitation of the remedy, it was not considered worth while to make an analysis of the preparation. Recently, however, an advertising campaign for the sale of the remedy has been inaugurated both in the lay and to a limited degree in the medical press. A quarter page advertisement has been appearing in medical journals often supplemented by a "reader" which still further sets forth the supposed merits of the nostrum. In the advertisements in the daily papers the assertion is made that Jaroma is indorsed by the medical profession and in support of this, parts of the "reading notices" from the medical journals are quoted.

The circulars accompanying the nostrum are evidently intended for the laity as may be seen from the following:

"Are you nervous? Take Jaroma Tablets."
"Can't you sleep? Take Jaroma Vegetable Tablets."
"Jaroma Vegetable Tablets, the new & wonderful specific for the 'American Disease' Nervousness in its various forms."
" . . . Jaroma is the needed special nerve food to counteract the special strain of modern American business and social life."
"For the discovery of the Jaroma formula we are indebted to an eminent German Nerve Specialist who has had most gratifying results from this compound in his private practice."

Jaroma having gone to the medical profession its examination was taken up by the Association's chemists who reported as follows:

LABORATORY REPORT

Narthex, the alleged source of Jaroma, is a nearly obsolete name for a genus of plants from some species of which the well-known drug asafetida is obtained. Physicians who are familiar with the origin or sources of drugs will have little difficulty in recognizing this substance from the mysterious description given in the "readers" that appear in certain medical journals, while no one could fail in identifying it by breaking one of the Jaroma tablets!

Jaroma is put up in tablet form in packages to be retailed at 10, 15 and 50 cents, the 10-cent size containing two, and the 50-cent size twelve of the tablets.

Qualitative tests demonstrated that the medicinal portion of the tablets consists of asafetida, calcium sulphate (gypsum) and powdered capsicum, the greater proportion consisting of the two former ingredients. The absence of hypnotic alkaloids, bromids and chloral was demonstrated and other hypnotics such as diethyl-barbituric acid (veronal) and sulphon methane (sulphonal) were not found. Although no exact quantitative separations were made it is believed that a tablet containing asafetida 3 grains, gypsum 2 grains and capsicum 1/10 grain, would have properties similar to Jaroma. As gypsum has been frequently employed as an adulterant of asafetida the analyst has no means of demonstrating whether the calcium sulphate found in the tablets had been added as a "make-weight" or whether it is a part of the "formula" of the "eminent German Nerve Specialist."

THE JOURNAL commented on the above report as follows:

Thus according to the chemists' report this "new vegetable hypnotic" and "special nerve food" is, essentially, asafetida. Although in rational medicine no hypnotic powers are claimed for this drug it is often prescribed in certain forms of hysteria, while as a condiment, it has been known and used from prehistoric times. Therefore, the only new thing about the

stuff is its name and the fraudulent use to which asafetida is put. Jaroma is another of those nostrums which are used to humbug both the public and the medical profession.

Details of Analysis

Five of the tablets when deprived of their coatings weighed 1.6630 gm. or 0.3326 gm. each, or about 5 grains each. The presence in the coating of cane sugar, calcium sulphate and starch was demonstrated by the usual tests. Qualitative tests indicated that the medicinal portion of the tablets contains asafetida, calcium sulphate and capsicum. Alkaloids, iodids and bromids were absent. Neither chloral nor other synthetic hypnotics were found.

Asafetida: On breaking one of the tablets a strong odor like asafetida was observed. One of the tablets was crushed in a mortar and the powder triturated with hydrochloric acid. The mixture was filtered and the filtrate made alkaline with ammonia water. A strong, bluish fluorescence indicated the presence of asafetida in the tablets. The coating was removed from one of the tablets, the remaining portion triturated with alcohol, the insoluble part allowed to settle and the solvent decanted through a filter. The insoluble material was again treated with alcohol and the treatment continued until exhaustion was complete. The solvent was evaporated and the residue dried at 100 C.

Result: One tablet weighing 0.3479 gm. gave 0.1154 gm. soluble matter, or 33.17 per cent. Another tablet weighing 0.3523 gm. gave 0.1212 gm. soluble matter, or 34.4 per cent.; average, 33.78 per cent. soluble matter. Assuming that the asafetida used was of the quality required by the U. S. P., i. e., containing 50 per cent. of alcohol-soluble matter, the asafetida present should amount to 67.5 per cent. of the weight of the medicinal portion of the tablets. Since the average weight of the uncoated tablets is about 0.3326 gm., the asafetida present in each tablet should amount to about 0.2247 gm., or 3.4 grains.

Capsicum: Capsicum was detected by treating an alcoholic extract of the powdered tablets by the method described by LaWall (*Am. Jour. Pharm.*, 1909, lxxxi, 218). The method is described on page 95. By this method the presence in the tablets of small quantities of capsicum was indicated. Microscopic examination of the powdered tablets showed that powdered capsicum was present in small amounts.

Chloral Hydrate: The absence of chloral hydrate was demonstrated by the following test: To 10 c.c. of an alcoholic solution from the tablets (representing 1 tablet), 100 c.c. of water and a few drops of nitric acid were added. The mixture was shaken with 50 c.c. of ether, the aqueous layer was withdrawn and heated to expel dissolved ether. The solution was then filtered and the filtrate tested for chlorid with silver nitrate test solution. Another portion of 10 c.c. of the above alcoholic solution was boiled for one hour in a reflux apparatus with 20 c.c. of half normal alcoholic potassium hydroxid. The solution was then evaporated to about 10 c.c., the residue diluted with 80 c.c. water, the solution acidified with nitric acid, shaken with ether, the aqueous layer removed, warmed, filtered and tested for chlorids. No apparent increase in cloudiness was produced by silver nitrate test solution, which was taken to indicate the absence of chloral hydrate in the tablets.

Diethyl-Barbituric Acid (Veronal): The absence of diethylbarbituric acid was indicated by the following test: One of the tablets was crushed and the powder heated for an hour on a water bath with a 25 per cent. solution of sodium carbonate. No blue color, indicative of ammonia, was produced on red litmus paper suspended in the vapors. The test depends on the property that ammonia is produced by prolonged heating of diethyl-barbituric acid with sodium carbonate solution.

Sulphonmethane (Sulphonal): The absence of sulphonmethane (sulphonal), sulphonethylmethane (trional) and similar substances was shown by the following test: An alcoholic extract from the tablets, representing 5 tablets, was boiled in a reflux apparatus with alcoholic potassium hydroxid. The solution was evaporated nearly to dryness, the residue taken up in 100 c.c. of water, the solution acidified with hydrochloric acid and the mixture extracted with ether. The ethereal solution was washed with water evaporated to dryness, the residue moistened with 10 c.c. alcohol and again evaporated to dryness. The residue was ignited with dry sodium acetate, the mass extracted with water, the solution filtered and the filtrate acidified with hydrochloric acid. No odor of hydrogen sulphid was observed which was taken to indicate the absence of complex sulphur compounds such as sulphonmethane, etc. A duplicate test to which 0.300 gm. sulphonmethane had been added previous to the first extraction with alcohol, gave an abundance of hydrogen sulphid.

Calcium Sulphate (Gypsum): The tablets were deprived of their coatings, the portion remaining ignited, the residue dissolved so far as possible in hot, diluted hydrochloric acid, the solution filtered and the calcium in the filtrate estimated by the oxalate method in the usual way, the substance being weighed as calcium carbonate.

Result: One tablet weighing 0.3024 gm. gave 0.0749 gm. calcium carbonate, equivalent to 0.12885 gm. crystallized calcium sulphate, or 43.61 per cent.; a duplicate weighing 0.3364 gm. gave 0.0852 gm. calcium carbonate, equivalent to 0.146569 gm. crystallized calcium sulphate or 43.57 per cent. Average, 43.09 per cent. crystallized calcium sulphate. This is equivalent to about 2 grains per tablet. Since the medicinal portion of the tablets weighs about 5 grains, and since no remaining constituents other than asafetida and capsicum could be found, and since the capsicum was shown by microscopical means to be present in very small amounts, it is concluded (by difference) that about 3 grains of asafetida is present in each tablet.

THE ANALYSIS OF URIKOL AND KYDNUS

(Abstracted from The Journal A. M. A., Oct. 7, 1911, p. 1222)

Urikol and Kydnus are nostrums sold by the Interstate Remedy Co., of Detroit, Mich. The method of their exploitation and the character of the firm selling it were fully considered in THE JOURNAL, A. M. A., Oct. 7, 1911, p. 1222. To make the exposé of this nostrum more complete, an analysis was made and reported in THE JOURNAL (loc. cit.) as follows:

Urikol.—The powder in the box labeled "Urikol" is greenish yellow in color and possesses an odor in which, among others, that of buchu is most prominent. Quantitative analysis yielded the following results:

Water-soluble matter	37.93 per cent.
Alcohol-soluble matter	9.55 per cent.
Chloroform-soluble matter	3.67 per cent.
Insoluble matter	52.96 per cent.
Moisture	5.20 per cent.
Undetermined	0.69 per cent.
	100.00

The portion soluble in water contains what appears to be sugar and some drug extracts, the most prominent appearing to be buchu. The alcohol-soluble part has in general the same properties as the water-soluble portion. The substance soluble in chloroform was identified as hexamethylenamin. The portion insoluble in the above solvents consists approximately

of equal parts of starch and calcium carbonate. The remainder of the powder is chiefly moisture. The presence of alkaloids, arsenic or metals could not be demonstrated.

From these results it appears that the powder called Urikol is essentially a small quantity of hexamethylenamin and some drug extracts in a mixture of starch, sugar and calcium carbonate.

Kydnus.—The powder in the box labeled "Kydnus" is light brown in color, possessing a taste and a slight odor of hydrogen sulphid. Quantitative analysis yielded the following:

Water-soluble matter	38.75	per cent.
Dilute acid-soluble matter	27.20	per cent.
Concentrated acid-soluble matter	2.94	per cent.
Insoluble matter	28.08	per cent.
Moisture	2.80	per cent.
Undetermined	0.23	per cent.
	100.00	

The portion soluble in water consists of about 32 per cent. sugar and the rest potassium and calcium sulphates. The acid soluble part consists of about 27 per cent. calcium carbonate and about 0.2 per cent. calcium sulphid. The portion soluble in concentrated acid consists of iron equivalent to about 3 per cent. ferric oxid. The residue insoluble in the above solvents is practically entirely starch. The remainder of the powder is chiefly moisture.

From these results it is concluded that Kydnus is essentially a mixture of calcium carbonate, starch and sugar containing a small quantity of calcium sulphid and iron.

THE JOURNAL commented on the analysis as follows:

As usual, of course, it is found that the nostrums used by these quacks are drugs that are in common use by regular physicians. It is the same old story. Well-known drugs enveloped in a cloud of secrecy and mystery, endowed with properties they do not possess and sold at a price enormously in excess of their worth.

REACTION OF POTASSIUM ARSENITE AND IODIN IN PRESENCE OF PHENOL

(*Abstracted from The Journal A. M. A., Nov. 18, 1911, p. 1713*)

An inquiry was received concerning the reaction and the new compounds formed, if any, in the following formula:

Liq. potassii arsenitis		
Tinct. iodii		
Phenolis	āā	♏ xvj
Aquæ	q. s. ad	℥j

The mixture was prepared according to the above formula and examined. As a result of the examination THE JOURNAL replied:

"In alkaline solution, iodin converts arsenites to arsenates, forms tri-iodophenol from phenol, and iodoform from alcohol, the latter two reactions taking place ordinarily in warm solutions. Experiments made by our chemists show that, in the present instance, only the arsenite is affected. The acid formed in the oxidation of the arsenite neutralizes the alkali, the solution becomes acid in reaction, and hence the chemical reaction stops, even before the arsenite is all oxidized. This was shown by the presence in the finished prescription of both an arsenite and an arsenate and by the facts that the solution was acid in reaction and contained free iodin. Assuming that solution of potassium arsenite (Fowler's solution) contains potassium arsenite (KH_2AsO_3) and potassium carbonate (K_2CO_3), the reactions which occur may be represented thus:

$$2KH_2AsO_3 + 2I_2 + 2H_2O \rightleftarrows K_2HAsO_4 + H_3AsO_4 + 4HI$$
$$2HI + K_2CO_3 \rightarrow 2KI + CO_2 + H_2O$$
$$H_3AsO_4 + K_2CO_3 \rightarrow K_2HAsO_4 + CO_2 + H_2O$$

"It would appear, then, that the only new compound which is formed is the arsenate produced by the oxidation of the trivalent arsenic in Fowler's solution.

"On standing, the solution became lighter in color and after a week the free iodin had almost completely disappeared. The solution still contained arsenic in both the trivalent and pentavalent condition. The chemists are unable to explain the reaction which caused the disappearance of the free iodid on standing."

THE ANALYSIS OF HESPERIAN TONIC

(Abstracted, with additions, from The Journal A. M. A., Nov. 25, 1911, p. 1780)

In the course of an article in THE JOURNAL A. M. A., in which the viciousness of the curative claims made for Hesperian Tonic were exposed, the claimed and actual composition of this product were compared. Regarding the claimed composition the following, giving the formula on the label and comments thereon was published:

Flussiges Eisenchlorid	Gm. 7.500
Versusster Salpetergust	Gm. 15.000
Distillerte Wasser	Gm. 7.500

To the unitiated, the apparent frankness of this formula may seem credible. Of course, not one layman in ten thousand will be any the wiser when he has read it than he was before. In plain English, the formula signifies that the preparation is a solution of ferric chlorid and spirits of nitrous ether in distilled water. The idea of publishing the composition in indifferent German is admittedly a master stroke of advertising trickery.

On the other hand the following résumé of the laboratory findings was published:

Hesperian Tonic is a brown liquid with an odor resembling spirits of nitrous ether. When slightly heated it easily ignites and continues to burn, indicating a relatively large percentage of alcohol. The liquid responded to tests which indicate the presence of alcohol, iron, chlorid, a trace of nitrite and some nitrate. The presence of arsenic, heavy metals and alkaloids could not be demonstrated. Quantitative analysis indicated the presence of alcohol equivalent to 33.72 per cent. U. S. P. alcohol by volume; and iron (Fe) 2.151 gm. per 100 c.c., equivalent to approximately 21.50 gm. liquor ferri chloridi, U. S. P. No nitrous ether (ethyl nitrite) was found although the odor of the preparation and the formula pointed to its presence. In view of the ease with which spirits of nitrous ether decomposes, this is not surprising. Experiments on mixtures of ferric chlorid solution and spirits of nitrous ether were made and showed that in such a mixture, the nitrous ether is decompased quite rapidly with reduction of some of the iron to the ferrous state and the formation of some nitrate. From this it is concluded that Hesperian Tonic is a water-alcohol solution of ferric chlorid with decomposition products of the spirits of nitrous ether, probably present originally.

These conclusions were based on work which is detailed below:

Details of Analysis

The odor of the preparation together with the formula printed on the label having suggested the presence of spirits of nitrous ether, tests were made to identify this substance as an ingredient. While it is well known that both nitrates and nitrites under proper conditions can oxidize iron in the ferrous condition, available literature gave no information regarding the interaction of ferric chlorid and spirits of nitrous ether, nor even the action of ferric iron on nitrites in general, therefore the tests made to study this point are given in considerable detail.

In commenting on the preceding paragraph, Prof. Alexander Smith, University of Chicago, to whom it was referred for criticism, suggested "that while nitric acid and ferric chlorid are of almost exactly the same activity as oxidizing agents in

aqua solution, they may not be so much alike in strongly alcoholic solution. In the latter circumstance the ferric chlorid seems to be the more active."

The preparation liberated iodin from a solution of potassium iodid, acidified with acetic acid (indicating the possible presence of nitrite) but no gas was simultaneously evolved and therefore it was thought possible that the liberation of iodin might be due to the presence of ferric iron, since qualitative tests as well as the formula, indicated the presence of iron. To rid the preparation of ferric iron it was treated with barium carbonate and then filtered. The clear and colorless filtrate when treated with a solution of potassium thiocyanate yielded but a faint pink color; ammonium hydroxid produced a greenish-white precipitate; potassium ferrocyanid yielded a bluish-white precipitate, and potassium ferricyanid yielded a dark-blue precipitate, and an acid solution of potassium permanganate was reduced.

These tests showed that this solution contained ferrous iron and practically no ferric iron. The solution was then tested with acidified potassium iodid solution, but only the faintest coloration appeared, indicating not more than a trace of nitrite.

Another sample treated with ammonia water (to rid the solution of all iron) the resulting precipitate filtered off, yielded a clear colorless solution which when made acid and then treated with acidified potassium iodid solution, yielded only a faint coloration; another portion treated with dilute acid and antipyrin solution yielded no green coloration; a third portion treated with alphanaphthylamine and sulphanilic acid yielded but a faint pink tint. These tests all indicated the absence of all but a trace of nitrite.

Experiments made on freshly prepared mixtures of ferrous sulphate, ferric chlorid and spirits nitrous ether, showed that the iron could be removed without hindering the nitrite reactions. Mixtures of this kind treated with ammonia water and filtered, yielded solutions responding to the various tests for nitrite, viz., liberated iodin from a solution of potassium iodid acidified with acetic acid, with evolution of gas; gave a green color with an acid antipyrin solution, and were colored a deep pink by alphanaphthylamine and sulphanilic acid.

Tests such as the ferrous iron and sulphuric acid ring test and the diphenylamin tests (after boiling with ammonium sulphate to destroy any nitrite possibly present) indicated the presence of nitrate. Further tests demonstrated the presence of small quantities of aldehyd. The presence of nitrate together with the very small amount of nitrite suggested that if spirits of nitrous ether had been present originally a transformation had taken place, viz., that the nitrite had been decomposed and to some extent converted to nitrate. To test

the truth of this assumption a mixture consisting of ferric chlorid solution, U. S. P. 25 c.c., spirits nitrous ether, U. S. P. 50 c.c. and water, 25 c.c., was allowed to stand for nearly a month and then tested side by side with (a) a fresh mixture of the same ingredients and (b) the preparation under examination. The odor of the mixture which had been allowed to stand was slightly different from the fresh mixture, but still strongly suggestive of spirits of nitrous ether.

Five c.c. of each of the above three solutions were treated with sodium hydroxid to saponify the ester, the ferric hydroxid filtered off and made up to 100 c.c. and 2 c.c. alphanaphthylamine solution and 2 c.c. sulphanilic acid added to each sample. The freshly prepared mixture of the iron salt and spirits nitrous ether yielded a deep pink color; the mixture which had stood for a month yielded only a very faint pink tint, but somewhat stronger than the preparation under examination. These results were taken to show that the ferric chlorid in contact with nitrous ether caused or hastened the decomposition of the latter, and that the preparation examined originally contained spirits of nitrous ether and ferric chlorid solution.

The total iron content of the preparation was determined by taking 25 c.c. portions and diluting to 500 c.c. and using 25 c.c. samples of this solution, in which iron was estimated in the usual way by boiling with bromin water, precipitating as the hydroxid, igniting and weighing as the oxid. In this way samples (a) yielded 0.0384 gm. ferric oxid, and (b) 0.0386 gm., an average of 0.0385 gm. ferric oxid. This is equivalent to approximately 21.50 gm. liquor ferri chloridi, U. S. P. per 100 c.c.

To determine the alcohol content 25 c.c. of the preparation was treated with silver nitrate and sodium hydroxid, allowed to stand two days to destroy aldehydes and then distilled; 25 c.c. of the distillate measuring 100 c.c. had a specific gravity of .9889, equivalent to 8.00 per cent. absolute alcohol by volume, equivalent to 33.72 per cent. U. S. P. alcohol by volume in the original preparation.

TIZ

A Cure for "Smelly Feet"—and Other Things

(*Abstracted from The Journal A. M. A., Dec. 2, 1911, p. 1853*)

A widely advertised toilet article, which is of a medicinal nature and about which THE JOURNAL has had numerous inquiries, is sold under the name of Tiz by Walter Luther Dodge & Co., Chicago.

A specimen of this preparation was examined and the following report published in THE JOURNAL:

"Tiz is sold in the form of tablets, of which a 25-cent package contains from twenty to twenty-five. Neither on the label of the package nor in the circular accompanying it is there any statement concerning the composition of the preparation. The tablets weigh about 1.14 gm. (17½ grains) each. Qualitative tests indicated the presence of aluminum, potassium, a sulphate, tannic acid, salicylic acid, powdered talcum and starch. Quantitative determinations of the aluminum, the sulphate and the salicylic acid were made. An approximate estimation of the sum of the starch and talcum was made by determining the portion insoluble both in water and in alcohol. From the loss on the ignition of this fraction the relative proportions of starch and talcum were estimated. From the results of the examination it is believed that a tablet having the following composition would have properties similar to Tiz:

Potassium aluminum sulphate (alum)	60 per cent.
Tannic acid	10 per cent.
Salicylic acid	5 per cent.
Talcum (Talc)	5 per cent.
Starch	20 per cent."

In discussing one of the testimonials used in exploiting this nostrum THE JOURNAL commented as follows:

"Of course, testimonials are used in true 'patent medicine' style. We learn, for instance, that Mrs. Crockett of Jeffersonville (state not mentioned) had been unable to walk down stairs for five years 'except by stepping down on each step with one foot at a time'—the intimation being, apparently, that most people walk down stairs with both feet at a time. In any case, we learn that 'after the second treatment she walked down stairs one foot at a time.' The lady's husband, who sends in this testimonial, closes by saying: 'This is remarkable. Send five more boxes.' Doubtless by the time the fifth box is used Mrs. Crockett will be spry enough to slide down the bannisters."

THE ANALYSIS OF SULPHUME

(Abstracted from The Journal A. M. A., Dec. 2, 1911, p. 1853)

Many years ago a preparation made by boiling lime and sulphur in water was introduced under the name of Vleminckx' solution as an internal application for certain skin diseases. Since its introduction it has been exploited as a wonderful "skin and blood" remedy disguised under various names: "sulphurine," "golden lotion," "yellow lotion," "liquid sulphur," "soluble sulphur" and "sulphume." As a type of these various aliases of Vleminckx' solution the nostrum "sulphume" made

by the "Sulphume Company," Boston, Mass., was analyzed. The results of this examination were summarized in THE JOURNAL A. M. A., Dec. 2, 1911, p. 1853, as follows:

"A package of Sulphume recently purchased bears the following legend:

'Sulphume for the skin and blood. The contents of this bottle makes 10 strong sulphur baths. Dose—Internally: Four to six drops of Sulphume in one half tumbler of water 3 times daily, one-half hour after meals. Price $1.00. Sulphume Company, Boston, U. S. A.'

"Accompanying the bottle is a booklet entitled 'Sulphur and Its Benefits to Health,' in which Sulphume is lauded for its value in treating all sorts of skin diseases, catarrh, corns, bunions, diabetes, diphtheria, female weakness, fevers, hemorrhoids, rheumatism, prostatitis, rickets, etc.

"The preparation as received in the laboratory is an orange-colored clear liquid, which on the addition of acid yields a precipitate of sulphur, accompanied by evolution of hydrogen sulphid. The liquid is alkaline toward litmus. Qualitative tests showed the presence of polysulphid, thiosulphate and calcium, but the absence of sulphate or sulphite.

"Quantitative determination showed the presence of about 1 gm. sulphur per 100 c.c. of Sulphume, in the form of thiosulphate, and about 4 gm., per 100 c.c., in the form of polysulphid, making a total of about 5 gm. sulphur per 100 c.c. of the preparation. The calcium content was found to be equal to 2.55 gm. calcium oxid (CaO) per 100 c.c. of Sulphume." .

These conclusions were based on the results of an analysis which is detailed as follows:

Details of Analysis

From its appearance and odor, and from the composition of similar preparations, it was suspected that Sulphume was a calcium polysulphid solution. The liberation of hydrogen sulphid and precipitation of sulphur on the addition of acid indicated the presence of polysulphids.

The presence of sulphites, thiosulphates and sulphates was also possible, and accordingly these substances were tested for. The polysulphids were removed by the addition of an excess of lead carbonate and the filtrate tested for thiosulphate, sulphite and sulphate. Since a solution of thiosulphate can be boiled with dilute acetic acid without decomposition, and sulphites under the same condition yield sulphur dioxid (*Chem. Centralbl.*, 1905, i, 950), and as the presence of thiosulphates was probable, this method was used to test for sulphites and thiosulphates.

When a sample of the filtrate from the precipitate formed by the addition of lead carbonate to Sulphume was boiled

with dilute acetic acid, no sulphur dioxid was evolved, indicating the absence of an appreciable quantity of sulphite. Another portion of the same filtrate when treated with iodin solution decolorized the latter; when heated with dilute hydrochloric acid sulphur dioxid was evolved and a precipitate of sulphur formed. These reactions showed the presence of thiosulphate.

Sulphate was tested for in undiluted Sulphume by adding barium chlorid solution; the absence of a precipitate indicated the absence of sulphate. To be sure that Sulphume had no inhibiting effect on the formation of barium sulphate, should sulphate be present, 0.5 c.c. of a 0.1 per cent. solution of potassium sulphate was added to a mixture of 5 c.c. Sulphume, 5 c.c. water and 2 c.c. barium chlorid solution (10 per cent.). This resulted in the formation of a white precipitate showing that 0.0005 gm. or 0.01 per cent. potassium sulphate could be detected in Sulphume. Qualitatively, then, Sulphume was found to contain polysulphids, thiosulphates, but no sulphites or sulphates.

To determine the polysulphid and thiosulphate, the method in Bull. 101, p. 9, Bureau of Chemistry, U. S. Department of Agriculture, was used. The polysulphid is precipitated by zinc chlorid solution, and the thiosulphate determined by titrating with iodin the filtrate from the sulphid precipitation. The precipitated sulphids, now in the form of zinc sulphid, are dissolved in a saturated solution of potassium hydroxid and then oxidized by hydrogen peroxid solution to sulphate, which is then determined as barium sulphite in the usual way.

By these methods the following results were obtained:

Ten c.c. of Sulphume were diluted and made up to 100 c.c. and 10 c.c. samples used in the following estimations: (a) Ten c.c. of the solution yielded 0.3008 gm. barium sulphate representing 4.23 gm. Sulphume as sulphids and polysulphids per 100 c.c. of Sulphume; (b) another sample yielded 0.2903 gm. barium sulphate, equivalent to 3.98 gm. sulphur per 100 c.c. Sulphume, an average of 4.10 gm.

The thiosulphate was estimated by titrating the filtrate from the precipitated sulphids and polysulphids from an undiluted sample and yielded the following results: (a) Five c.c. of the Sulphume treated as above required 8.11 c.c. tenth-normal iodin; (b) 5 c.c. Sulphume required 8.09 c.c. tenth-normal iodin; an average of 8.10 c.c., equivalent to 1.08 gm. sulphur as thiosulphate per 100 c.c. Sulphume.

The sulphid in Sulphume was estimated by titration of Sulphume directly with iodin and thiosulphate. A measured volume of Sulphume was added to an excess of tenth-normal iodin solution and the excess of iodin titrated by thiosulphate. As the solution contains thiosulphate the amount of iodin consumed represents the thiosulphate *plus* the sulphid present and knowing the thiosulphate content the sulphidic sulphur

may be calculated. Thus (a) 5 c.c. Sulphume requires 33.49 c.c. tenth-normal iodin; (b) 5 c.c. requires 33.51 tenth normal iodin or an average of 33.50 c.c. iodin. After removing sulphids, etc. by zinc chlorid 5 c.c. of the preparation required an average of 8.10 c.c. iodin. As 33.50 c.c. represents the iodin consumed by the sulphid *plus* the thiosulphate in 5 c.c. of Sulphume, 33.50 minus 8.10 c.c. or 25.40 c.c. represents the sulphur present as sulphid; or 0.80 gm. per 100 c.c. Sulphume.

The total sulphid and polysulphid sulphur was estimated by separating the sulphur precipitate after the addition of an excess of iodin to Sulphume, washing and dissolving in chloroform, filtering, evaporating and weighing the residue. By this method the following results were obtained: (a) 5 c.c. yielded 0.2026 gm. sulphur and (b) 5 c.c. yielded 0.2034 gm. sulphur, an average of 4.06 gm. per 100 c.c., agreeing with the sulphid and polysulphid sulphur content (4.10 gm. per 100 c.c.) determined by the peroxid method.

Total sulphur was estimated by adding diluted Sulphume to a strong solution of sodium peroxid and allowing to react and acidfying and precipitating the sulphate as barium sulphate. Thus 10 c.c. Sulphume diluted to 100 c.c. and 10 c.c. portions used yielded (a) 0.3716 gm. barium sulphate, equivalent to 5.12 gm. sulphur per 100 c.c. Sulphume; (b) 0.3710 gm. barium sulphate, equivalent to 5.08 gm.; and average of 5.10 gm. sulphur per 100 c.c. Sulphume.

For convenience of comparison the results are herewith tabulated:

SULPHUR PER 100 C.C. SULPHUME IN THE FORM OF

	Gm.
Thiosulphate	1.08
Sulphid	0.80
Sulphid plus polysulphid (by iodin)	4.06
Sulphid and polysulphid (by hydrogen peroxid)	4.10
Total sulphur (by addition)	5.16
Total sulphur (by peroxid method)	5.10

THE ANAYLSIS OF OXIDAZE

(Abstracted, with additions, from The Journal A. M. A., Dec. 30, 1911)

An article in THE JOURNAL A. M. A. (loc. cit.), on "oxidaze" brought out the similarity of this nostrum to Oleozone and Hydrocine; each some time ago exposed (THE JOURNAL A. M. A., March 20, 1909, p. 576) as "an odoriferous sugar mixture sold under many names and by various persons as a tuberculosis cure." The articles included a report of analysis made in the Association laboratory of "Oxidaze" as sold to the public to-day. The following is the report:

"The tablets received in a carton labelled 'Oxidaze Tablets No. 1 Dark. A most effective remedy in the treatment of Tuberculosis, Pneumonia, Asthma . . . etc. . . . prepared

tor American Oxidaze Company, Worcester, Mass.," are dark brown in color possessing a strong odor and taste of essential oils. A general separation of ingredients yielded the following results:

Chloroform-soluble matter	10.98 per cent.
Water-soluble matter	7.86 per cent.
Water-soluble matter (by difference)..	81.16 per cent.
	100.00

"The chloroform-soluble matter appears to be, at least in large part, a mixture of volatile oils.

"The water-soluble portion appears to consist of sugar containing some dye and a trace of potassium iodid, the latter amounting to 0.14 per cent. of the tablet.

"The water-insoluble matter consists almost entirely of corn starch.

"The specimen of Oxidaze tablets examined may then be said to consist essentially of sugar containing a small amount of volatile oils, starch and a trace of potassium iodid."

When treated with water the tablets disintegrated forming a solution containing a small quantity of suspended matter and floating on its surface some oily drops. Chloroform or ether extracts from either the dry tablets or the aqueous solution practically all the odorous ingredients; and after removing the solvent from the residue, left after treating the dry tablets with chloroform, water dissolves the greater part of the material, leaving a small percentage of matter insoluble in water.

An approximate determination of the chloroform-soluble matter was made by placing on a weighed filter a weighed quantity of the powdered tablets and percolating with chloroform until the percolate on evaporation no longer left a residue. The filter and contents were then weighed after drying at 100° C. to constant weight. The loss was recorded as chloroform-soluble matter. The following results were obtained: (*a*) 1.3273 gm. material after percolation and drying to constant weight was found to have lost 0.1357 gm. or 11.06 per cent. of the material taken. In the same way (*b*) 1.4521 gm. tablets lost 0.1583 gm. or 10.90 per cent., an average of 10.98 per cent.

The water-soluble matter was determined by percolating the residues left by the chloroform percolation with water and again drying and weighing the residue. Thus (*a*) 1.3273 gm. material lost 1.0768 gm. or 81.12 per cent., and (*b*) 1.4521 gm. material lost 1.1790 gm. or 81.20 per cent., an average of 81.16 per cent.

The water-soluble matter reducing Fehling's solution directly and to a much greater extent after boiling with hydrochloric acid indicated the presence of sucrose admixed with its decomposition product, invert sugar. Determinations on the

water-soluble matter freed from starch and essential oils, carried out according to the details given in the official methods of the Bureau of Chemistry, Department of Agriculture (Bull. 107, p. 242), indicated the presence of 3.06 per cent. invert sugar and 77.27 per cent. sucrose; a total of 80.33 per cent. sugar which demonstrated that the water-soluble portion consists almost entirely of sucrose and invert sugar. As a check, the sugar in the water-soluble portion of 6.5410 gm. material, representing about 5 gm. sugar, was determined by the polariscope. Two operators read the rotation as (*a*) 3.33 and (*b*) 3.38 respectively—indicating 79.49 per cent. and 76.43 per cent. sucrose. This difference of 3.06 per cent. as is seen is a difference of only 0.05 degrees in the readings, due to the small amount of material used for this determination. The results in general check those given by chemical methods.

The residue left after chloroform and water percolations was recorded as the water-insoluble matter. Thus (*a*) 1.3275 gm. material yielded 0.1038 gm. or 7.82 per cent.; (*b*) 1.4521 gm. material yielded 0.1147 gm. or 7.90 per cent. residue, an average of 7.86 per cent. This residue under the microscope was identified as corn starch.

Since formerly pancreatin was claimed to be a constituent of similar tablets and since at that time an amount of nitrogen was found conforming to these claims, it was decided to determine whether or not pancreatin was a constituent of oxidaze tablets. Accordingly a sample was assayed for nitrogen by the Kjeldahl method and was found to contain only a trace of nitrogen, indicating the practical absence of pancreatin.

The following are the results of the nitrogen determinations: (*a*) 1.8104 gm. material yielded ammonia requiring 0.03 c.c. tenth normal acid, equivalent to 0.00004179 gm. nitrogen or 0.002 per cent.; (*b*) 2.0759 gm. material required 0.05 c.c tenth normal acid equivalent to 0.000069655 gm. or 0.003 per cent. nitrogen.

PART III.

REPORTS NOT PREVIOUSLY PUBLISHED

ARECA

The Committee on the American Pharmaceutical Association on Standards of Crude Drugs and Chemical Products having considered "Areca" the subject was assigned to the director of the chemical laboratory as referee for the preparation of tentative standards.

A tentative description of areca, based largely on the available literature, was prepared. Two specimens of the powdered drug, one of which was purchased and the other kindly furnished by Prof. Henry Kraemer of Philadelphia, were also examined and the results considered in the proposed standards.

The assay method is essentially that of the Swiss Pharmacopeia, but modified so that all liquids are measured. The method is most crude in that the total alkaloids are calculated by an arbitrary factor, and in that the larger proportion of the total alkaloidal content is generally believed to be inert, i. e., only about one-fifth of the total alkaloidal content consists of the physiologically active alkaloid, arecoline. However, since it has been deemed worth while to describe areca, although a drug of but little importance, it seemed best to include an alkaloidal standard with the other requirements. Hence the proposed standard of 0.5 per cent. of total alkaloids is probably better than no alkaloidal standard at all.

When examined by the methods given below the two specimens gave the following results:

Market Specimen: From 1.0007 gm. of the drug 0.0157 gm. ash was obtained, equivalent to 1.57 per cent.; from 1.0061 gm. of the drug 0.0152 gm. ash was obtained, equivalent to 1.51 per cent.; average, 1.54 per cent. ash. The alkaloids from the assay of duplicate specimens required respectively 14.0 c.c. and 14.21 c.c. of fiftieth normal hydrochloric acid, equivalent respectively to 0.0434 gm. and 0.0441 gm. areca alkaloids. Average, 0.04375 gm. areca alkaloids or 0.4375 per cent.

Kraemer Specimen: From 1.0012 gm. of the drug, 0.0157 gm. ash was obtained, equivalent to 1.57 per cent.; from

1.0039 gm. of the drug 0.0170 gm. ash was obtained, equivalent to 1.69 per cent.; average, 1.63 per cent. ash. The alkaloids from the assay of duplicate specimens required respectively 16.84 c.c. and 16.64 c.c. of fiftieth-normal hydrochloric acid, equivalent respectively to 0.0522 gm. and 0.0516 gm. areca alkaloids. Average 0.519 gm. areca alkaloids or 0.519 per cent. The results are herewith arranged in tabular form:

Source of Specimen	Ash			Alkaloid		
	a	b	Mean	a	b	Mean
Market	1.57	1.51	1.54	0.434	0.441	0.438
Kraemer	1.57	1.69	1.63	0.522	0.516	0.519

The following description and standards for areca are suggested:

AREKA

The seed of *Areca catechu* L. (Fam. Palmæ), yielding when assayed by the process given below not less than 0.5 per cent. of areca alkaloids.

From 20 to 25 mm. long, conical, greyish-brown with numerous spiral, reddish, depressed veins running chiefly from the hilum; hard; heavy; odorless, or faintly aromatic when broken; taste astringent, bitter and slightly acrid. A transverse section exhibits a marbled appearance, dark brown lines alternating with white portions, the former being folds of the seed coat, and the latter the endosperm.

If 1 gm. areca be ignited in a porcelain crucible the residue should not amount to more than 0.020 gm. (limit of *ash*).

ASSAY OF AREKA

Areca, in No. 60 powder, *fifteen grammes*	15 gm.
Chloroform, *one hundred and fifty cubic centimeters*	150 c.c.
Ether, *thirty-five cubic centimeters*	35 c.c.
Ammonia water, *ten cubic centimeters*	10 c.c.
Distilled water, *fifteen cubic centimeters*	15 c.c.
Fiftieth normal hydrochloric acid	
Hæmatoxylin test solution, each, *a sufficient quantity.*	

Place 15 gm. areca in a 250 c.c. Ehrlenmeyer flask and add 150 c.c. of a mixture composed of 1 volume of chloroform and 4 volumes of ether, the mixture having been cooled to 20 C. before measuring. Stopper the flask securely, and let it stand ten minutes. Add 10 c.c. of ammonia water and shake the flask vigorously every ten minutes for two hours. Add 15 c.c. of water, agitate, and place the flask in water at 20 C. for 15 minutes. Pour 100 c.c. of the clear liquid, representing

10 gm. of areca, through a dry filter into a graduated cylinder, transfer the solution to a 250 c.c. Erlenmeyer flask, wash the filter and graduated cylinder with 25 c.c. of the chloroform-ether mixture, adding the washings to the measured solution, evaporate or distill off the solvent and dissolve the residue in 5 c.c. of absolute alcohol. Add 30 c.c. of ether, 10 c.c. of water and 5 drops of hematoxylin test solution to the solution, and titrate with fiftieth-normal hydrochloric acid until the water solution is of a reddish-brown color. Then add 30 c.c. of water and continue the titration until the aqueous layer becomes of a citron-yellow color, or until further addition of acid fails to clarify the liquid. Each c.c. of fiftieth-normal hydrochloric acid consumed is assumed as equivalent to 0.0031 gm. of the mixed alkaloids of areca.

KERATIN

The director of the laboratory having been requested by the Chairman of the Committee of the American Pharmaceutical Association for Standards of Unofficial Drugs and Chemical Products to act as referee for Keratin, a provisional academic description was prepared as follows:

KERATIN—KERATINUM

Keratin is the horny substance of horns, hoofs, etc., of animals, purified by extraction with alcohol and ether and subsequent digestion with acid-pepsin solutions.

Keratin occurs as a brownish-yellow powder or in transparent white, or grayish white scales, which are tasteless and odorless. It is soluble in concentrated acetic acid, caustic alkalies and ammonia, but insoluble in water, alcohol, ether, dilute acetic acid or acid-pepsin solutions. It is decomposed by long boiling under pressure, forming a turbid solution with the liberation of hydrogen sulphid. Boiling with dilute sulphuric acid converts it to leucin, tyrosin and other products. On ignition it emits the odor of burning feathers and the remaining carbon is very difficultly burned.

If digested with fifteen times its weight of ammonia water or glacial acetic acid for twenty-four hours at 25 to 40 C. (77 to 104 F.) keratin should not leave more than 0.3 per cent. insoluble matter.

If 1 gm. of keratin be extracted with 25 c.c. of ether the etheral solution on evaporation should leave a residue corresponding to not more than 1 per cent. of the substance taken.

If 1 gm. of keratin be digested with 0.1 gm. of pepsin and 100 c.c. of water containing 3 c.c. of diluted hydrochloric acid at 55 C. (131 F.) for three hours, the filtrate evaporated to dryness and the residue dried to constant weight at 100 C. (212 F.), it should yield a residue weighing not more than 0.2 gm.

If 1 gm. of keratin be incinerated the ash should amount to not more than 0.3 per cent.

This description was submitted to the following firms for criticism:

Lehn & Fink
Mallinckrodt Chemical Works
McKesson & Robbins
Merck & Co.
H. K. Mulford & Co.
Parke, Davis & Co.
Powers-Weightman-Rosengarten Co.
Schieffelin & Co.
Sharp & Dohme
Frederic Stearns & Co.

At the same time the firms were invited to send specimens of their products for examination. In general no criticisms were received. Lehn & Fink, particularly gave careful consideration to the description and even submitted it to their correspondent abroad and in the end said:

"We submitted same to our chemist at our laboratory and also communicated with a prominent manufacturer of peptone and keratin in Germany in regard to this matter. No criticisms or suggestions, however, have been offered and the descriptions have been considered entirely satisfactory."

The firm sold a specimen of their product to the laboratory (at $2.75 per ounce). As no other specimen of stated source could be obtained the tests in the provisional description were applied only to this specimen. The acid-pepsin test as given in the provisional description having been carried out and a residue many times larger than was permissible having been found, the method was checked by estimating the acid-pepsin indigestible portion, i. e., the portion insoluble in the acid-pepsin solution. The value for the digestible portion was then obtained indirectly by subtraction from 100 per cent. The results are given herewith:

Acid-pepsin (indigestible) residue	1.27 per cent.
Acid-pepsin (digestible) residue	1.2295 gm.
Acid-pepsin (digestible) residue (by difference)	98.73 per cent.
Ammonia insoluble	1.73 per cent.
Ash	1.02 per cent.
Ether-soluble	0.51 per cent.

The results show that the specimen examined does not comply with the tests proposed, even though the letter of Messrs Lehn & Fink justified such an expectation. Particular attention is called to the fact that the specimen is almost entirely (98.73 per cent.) digestible in acid-pepsin solution. The findings of the experiments are in accord with those of Martindale and Westcot (Extra Pharmacopeia, ed. 14, 540, 1910) who investigated the efficiency of Keratin as a coating for pills and showed its worthlessness.

In view of these results the referee recommended that no monograph on Keratin be adopted. He further recommended

that the information be communicated to the National Formulary Committee so that this body might consider the desirability of omitting from the National Formulary the chapter on the coating of pills with Keratin.

Details of Analysis

The tests were carried out as described in the previous tests described above.

Acid-Pepsin (Digestible) Residue: One gm. of the material was digested with 100 c.c. of 0.3 per cent. hydrochloric acid and 0.100 gm. of pepsin for three hours at a temperature of 55 C. The mixture was diluted to 200 c.c. and allowed to settle over night. The mixture was then filtered and 100 c.c. of the clear filtrate evaporated to dryness. In one experiment 100 c.c. of the filtrate gave a residue weighing 0.6167 gm., equivalent to 1.2334 gm. for the entire sample taken. In another experiment 100 c.c. of the filtrate gave 0.6128 gm. residue, equivalent to 1.2256 gm. for the entire sample taken. Average, 1.2295 gm. Since but 1 gm. of material was taken for the test, the result cannot well be expressed in percentages.

Acid-Pepsin (indigestible) Residue: The portion of the material which was insoluble in one of the above digestion experiments was collected in a weighed Gooch crucible, dried and weighed. In one experiment a residue of 0.0127 gm. was obtained, equivalent to 1.27 per cent.

Ammonia Insoluble: One gm. gave an ammonia insoluble residue of 0.0193 gm., equivalent to 1.93 per cent.; a duplicate gave 0.0153 gm., equivalent to 1.53 per cent.; average 1.73 per cent. of ammonia insoluble substance.

Ash: From 1.0013 gm. of the material 0.0100 gm. ash was obtained, equivalent to 1.00 per cent.; 1.0011 gm. gave 0.0104 gm. ash, equivalent to 1.04 per cent.; average, 1.02 per cent.

Ether-Soluble: One gm. gave an ether-soluble residue of 0.0057 gm., equivalent to 0.57 per cent.; a duplicate gave 0.0046 gm. residue, equivalent to 0.46 per cent.; average 0.51 per cent. ether-soluble residue.

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